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Environmental Secondhand Smoke Exposure Triggered the Old Man Heart Adaptive Responses

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ABSTRACT

Secondhand Smoke (SHS) exposure has been linked harmful health outcome which is an important cause of short-lifespan morbidity and mortality. However, it is not clear pathological condition in old man exposure to SHS. This report reviews SHS exposure to old age to determine health mechanisms of the heart. SHS exposure increases the primary progressive atherosclerosis and arterial stiffness and increase risk of coronary disease events causes human diseases, especially in elderly. Aging is a physiology process involving progressive impairment of normal heart functions, due to an increasing vulnerability which reduces the ability of survive. Aging of the very elderly heart is associated with heart failure, expected or normal aging change. SHS exposure involves the combination of the smoke emitted by the burning end of a tobacco cigarette and the smoke exhaled by the smoker into the environment. SHS led to cardiac remodeling has been observed in exposed increases cardiovascular diseases mortality. Even for the elderly exposed to SHS at home was higher than outside of the home, or both at home and outside of the home. Experimental evidence in animal models has indicated attenuation in cardioprotective pathways with aging, yet information regarding myocardial dysfunction in elderly age is limited. Therefore, the numerous molecular and biochemical changes also affect the expression levels of human aging cardiac mitochondrial complex phenotype.

KEYWORDS

Secondhand smoke, Coronary disease, Cardiovascular diseases, Cardio protective pathways, Myocardial dysfunction, Molecular and Biochemical changes, Myocardial dysfunction

INTRODUCTION

Secondhand Smoke (SHS) exposure increases the risk of heart disease, including progressive atherosclerosis, decreased heart rate variability, increased arterial stiffness, and increased risk of coronary disease events. Left ventricular hypertrophy, a condition that has been observed in rabbits exposed to SHS, leads to ventricular remodeling and increases the risk of cardiovascular events and mortality. Even for young students, 25.7% were exposed to SHS at home, 34.2% outside of the home and 18.3% both at home and outside of the home. Old age is a strong independent predictor of death and morbidity in patients with structural heart disease. Therefore, old age is a major risk factor that is associated with poor cardiovascular outcome and that reduces endogenous cardio-protection. Both the incidence and the severity of atherosclerosis and cardiovascular disease increase with age. The changes to the heart throughout life are the result of maturational changes beyond sexual maturity, which cause hypertrophy of myocytes and hyperplasia of capillary endothelial cells and interstitial fibroblasts. Human cardiac aging generates a complex phenotype. Similar data are available regarding age-related changes in the human heart. SHS exposure is always associated with age, especially in old age. Age-related changes in an old-aged but otherwise normal heart mimic those changes associated with cardiac diseases, including myocardial infarction, aortic regurgitation, and alterations to cardiac valves and coronary arteries. Age affects cardiovascular function in the same manner as SHS exposure. Age-related changes in left ventricular morphology and function including decreased myocyte number, increased myocyte size, increased left ventricular wall thickness, and decreased conduction fiber density, while functional alterations include a decrease in intrinsic contractility, increased myocardial contraction time, decreased myocardial contraction velocity, and increased myocardial stiffness in left ventricular function. Age affects cardiovascular function in the same manner as SHS exposure. However, aging also shows relative adaptive responsiveness to eliminate damaged and exhausted cells from birth to senescence.

Heart failure due to SHS exposure was observed in old-age patients, which leads to heart remodeling and loss of function. Left ventricular hypertrophy (LVH) is an initial adaptive response. There are many compensatory mechanisms that respond to increased cardiac workload, sustained left ventricular stimulation being one of them. During LVH development, there is an imbalance of progressive remodeling at the cellular level. Therefore, we aim to further describe the molecular mechanisms involved in SHS exposure in the elderly to identify the pathological underpinnings of cardiac disease and disorders [1-8].

SHS exposure

Secondhand smoke (SHS) exposure is associated with elevated risks of Coronary Heart Disease (CHD) and stroke. The risks associated with high SHS exposure were very similar to risks from light active smoking, despite the much greater exposure to tobacco smoke in active smoking. The mechanisms by which SHS exposure elevates CHD risk remain uncertain. However, acute SHS exposure has been shown to increase platelet activity. Experimental data also suggest that SHS may cause endothelial damage, increasing endothelial cell turnover and causing a similar degree of endothelial dysfunction to that observed in active smokers. Active cigarette smoking influences all these pathways. SHS exposure always make human pathological cardiac hypertrophy, but smoking environment in old age health is still unclear. In left ventricular individual, SHS exposure may stimuli first a phase of cardiac hypertrophy. LVH has been observed in rabbits exposed to SHS. LVH leads to ventricular remodeling and increases the risk of a cardiovascular event and mortality. However, old age is a significant risk factor for Cardiovascular Diseases (CVDs). Extracellular Matrix (ECM) remodeling is an essential process to lead cardiac fibrosis. At time, the extracellular in the left ventricular is now as an essential dynamic participant in remodeling. Cardiac fibrosis is the consequences of the disruption of the equilibrium between the synthesis and degradation of collagen molecules. Myocardial fibrosis is results in an excessive accumulation of collagen fibers. SHS increases arterial stiffness and coronary cardiac disease events. That because of SHS exposure involves the combination of the smoke emitted by the burning end of a tobacco cigarette and the smoke exhaled by the smoker into the environment. Left ventricular pathological hypertrophy due to SHS exposure was observed in old-age patients, which leads to left ventricular remodeling and loss of function. LVH is an initial adaptive response. There are many compensatory mechanisms that respond to increased cardiac workload, sustained left ventricular stimulation being one of them. During LVH development, there is an imbalance of progressive remodeling at the cellular level, involving cardiomyocyte survival and cell death, or cell loss due to mitochondrial damage. Therefore, we describe the molecular mechanisms involved in SHS exposure to identify the pathological underpinnings of cardiac disease and disorders. In present demonstrate main cardiac hypertrophy signaling pathways, including IGF-II/IGF-IIR/Gαq/calcineurin/NFAT, IL-6/MEK5/ERK5 cascade and MEK1/ERK1/2-GATA4 and JAK1/2-STAT1/3 signaling pathways. Calcineurin/NFAT is an originally implicated as pathological hypertrophy signaling pathway. On the other hand, calcineurin/NFAT is regulated by MAPKs cascades mediated directly and indirectly. Therefore, calcineurin/NFAT regulate cardiac hypertrophy is associated with MEK1-ERK1/2 and MEK5/ERK5 signaling pathways. The subclassified branches IL-6/MEK5/ERK5 pathways which have been implicated in eccentric hypertrophy and death regulation in the heart. In addition, IL6/MEK5/ERK5 regulates MEK1-ERK1/2 and JAK1/2-STAT1/3 to regulate myocytes growth, apoptosis and contractile function. IL-6 is a pro-inflammatory cytokine, promoting tissue injury and cardiovascular pathologies. IL-6 after binding its gp130 receptor, lead to cardiomyocyte hypertrophy, increased fibrosis and heart failure. In contrast, the JAK/STAT pathway has been elucidated to late essential preconditioning of the heart as well as in cardiac hypertrophy, especially in pathological hypertrophy proves heart function rupture [1-12].

Aging exposure to SHS exposure

Aging is a human inevitable adaptive response to exhausted cell, while others regard it as a process that starts at conception and continues until death. Biologists consider aging to be a human physiologic change which has the slowly progressive structural changes and loss in body function with age. Cardiac aging is defined as the structural changes and functional declines with the onset of disease or degradation, but in the absence of environmental factors major cardiovascular risks such as smoking, hypertension, diabetes, and hypercholesterolemia. SHS and aging caused synergistic effects on the activation of heart adaptive mechanism (Figure 1). Genetics and epigenetics also leads to cardiovascular disease such as heart failure and atherosclerosis. However, aging shows relative adaptive responsiveness to eliminate damaged and exhausted cells from birth to senescence. A normal aging heart change which occurs mainly through from birth to senescence can produce mimic cardiac diseases, including coronary arteries, myocardial infarction, cardiac valves, aortic regurgitation, which is different with heart damage and adaptive response to eliminative damaged and exhausted cells. The aging changes of the elderly heart with LVH, which is expected and normal aging change. However, SHS exposure is associated with pathological LVH. Therefore, the effect of SHS exposure in the aged heart is interesting to be revealed. Cardiac aging is a human physiologic change which has the slowly progressive structural changes and functional declines with age, however, which have to in the absence of major cardiovascular risks such as high blood pressure. The physiologic changes of the aging cardiac include left ventricular hypertrophy, increased cardiac fibrosis and value degeneration. However, cardiovascular disease is a major risk factor for aging cause of death. Aging changes of the elderly heart is associated with physiological LVH, which is expected or normal aging changes, however, SHS exposure is associated with pathological LVH. SHS maybe leads to cardiovascular diseases such as heart failure and atherosclerosis. Besides, the effect of SHS exposure in aged heart is still unclear. Cardiac hypertrophy is a related change in cardiac morphology, including decreased in myocyte number, increased in myocytes size, decreased in matrix connective tissue, increased in left ventricular wall thickness, decreased in conduction fiber density and decreased in sinus node cell number. SHS exposure may stimuli first induce a phase of cardiac hypertrophy, especially in left ventricular individual. Certain normal aging changes may produce clinical heart

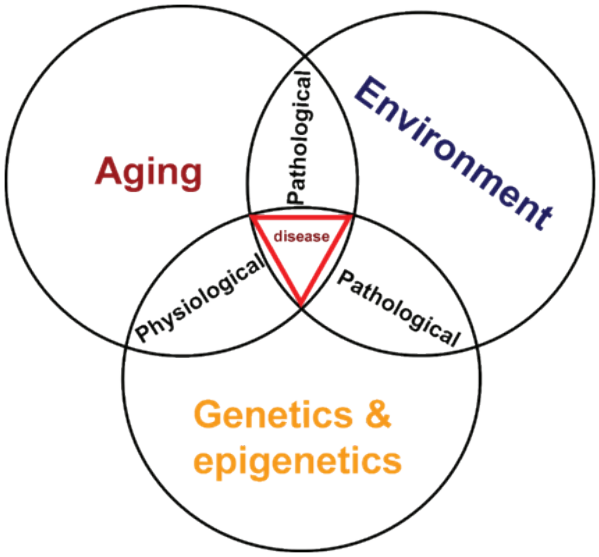

Figure 1: Aging is a physiological process involving progressive impairment of normal functions, due to an increasing vulnerability to injuries, which reduces the ability of the organism to survive. Obviously, this impairment takes place in a different manner depending on cell type and species. Dietary and environmental factors is the underlying effects of added diseases to analyze the normal aging process is very difficult.

disease and may mimic heart disease, such as cardiomyopathy, aortic valve calcium and mitral valve annular calcium. We found that changes associated with aging lead to cardiovascular pathological outcomes and the same cardiac adaptations that result from exposure to SHS. We found similar changes in cardiac morphology in aging rats and rats that underwent SHS exposure. We observed left ventricular chamber narrowing and rupture and increased left ventricular wall thickness. These results demonstrated left ventricular hypertrophy in aging rats and in SHS-exposed rats. Furthermore, we evaluated left ventricular function and left ventricular dimension, posterior wall thickness, interventricular septal at end-systole and end-diastole by echocardiography analysis. The results showed that left ventricular function in both aging rats and in SHS–exposed rats were lower than normal. Additionally, Left Wall Dimension (LVIDs), Posterior (LVPWs), Interventricular Septal (IVSs) at end-systolic were increased, but the end-diastolic only increased in the left wall dimension. According to our results, we determined that left ventricular hypertrophy was present. Interestingly, we found that EF (%) and FS (%) were compensated in young rats at 4 weeks of SHS exposure, but not in old age rats. At this time point, the heart changes associated with age may mimic heart disease, such as cardiac hypertrophy and heart failure. Aging leads to parallel stiffening of the aorta and heart, which causes an increase in systolic stiffness, contractility and diastolic stiffness. For 4 weeks of SHS exposure to fine particulate matter led to an increase in polymorphonuclear leukocyte cells. In the aging heart, left ventricular myocytes are constantly replaced by newly formed myocytes from birth to death. This process of aging offers an extraordinary example of the effects that the dynamic balance between cell death and cell growth has on the physiological and pathological restructuring of the heart. In the normal heart, the rate of cell death increases with age and is not balanced by new myocyte formation. The viable myocytes become hypertrophic to preserve myocardial mass in an aging heart. Thus, myocyte death, hypertrophy, and new myocyte formation characterize the aging heart. Cell apoptosis is involved in mitochondrial-dependent and mitochondrial-independent pathways. Two apoptosis pathways are consistently observed either in the aging or SHS hearts and are even more activated in aging and SHS hearts. Apoptosis has been reported to contribute to the loss of cardiomyocytes and is a recognized mechanism that may be involved in the control of cell proliferation. An increase in the Bad/Bcl2 ratio elevated mitochondrial membrane pore permeability, thus increasing cytochrome c release, and subsequent caspase-9 and caspase-3 activation to promote apoptosis. Several studies have shown that secondhand smoke exposure leads to an increased risk of cardiovascular disease. Moreover, the SHS and aging caused the synergistic activating increase in the Bad/Bcl2 ratio, elevating mitochondrial membrane pore permeability. This increased cytochrome c release and subsequent caspase-9 and caspase-3 activation to promote cell death in the heart. Additionally, cytokine/Fas receptor-driven pathways for cardiomyocyte apoptosis should also be taken into consideration. In contrast, we found that while aging myocytes are more prone to activate the cell death signaling pathway, younger cells possess hypertrophic ability and are less susceptible to cell death. Protein expression of constituents of the TNFα/Fas-L and Fas/FADD signaling pathways were consistently increased in the hearts of aging rats and SHS-exposed rats and were even more highly activated in the hearts of aging rats that were also exposed to SHS. Similarly, cleaved-caspase 8 was activated in young rats exposed to SHS, old rats exposed to SHS and old control rats. Activated caspase 8 cleaves Bid to form t-Bid and leads t-Bid to bind to mitochondrial membranes. We found that expression of t-Bid and Bid was increased in young rats exposed to SHS, old rats exposed to SHS, and old control rats. Finally, the occurrence of apoptosis is due to a death-survival imbalance in the aging process. The PI3K/AKT pathway delivers a survival signal, which is mediated by growth factors such as IGF-I and its receptor, IGF-IR. IGF-I exhibited a potent anti-apoptotic property through the anti-apoptotic member of the Bcl2 family and PI3K-transduced survival signals and their downstream signaling cascade after the activation of AKT and inactivation of Bad. This process only occurred in young SHS-exposed rats and not in aging or aging-plus-SHS-exposure rats. Similar results were observed in our previous report, which revealed an anti-hypertrophic effect of exercise training in rat hearts. In the young heart, the p-IGF1R survival pathway is more easily stimulated than in older animals. Overall, we believe SHS and aging both enhanced left ventricular hypertrophy. These results indicate that SHS exposure and aging induce upregulation of mitochondria-dependent and –independent apoptosis signaling pathways and downregulation of survival signaling pathways. Moreover, aging reduces IGF-I compensated signaling and accelerates the cardiac apoptotic effects induced by second-hand smoke. Aging and SHS should both be considered as risk factors for cardiac dysfunction. There are a lot of evidences indicated that SHS is a formidable health hazard. Because of a toxic air contaminant cause annual lung cancer and cardiovascular disease. Over the past few years publish papers we make a defined cardiac aging is human physiologic changes which has functional declines and the slowly progressive structural changes with aging, in the absence of major cardiovascular risks. Normal aging process is a physiologic process from birth to aging. It is possible that the aging of the coronary arteries is easily developed cardiac valves and coronary stenotic which will affect the cardiovascular system. In some papers elucidate aging affect the cardiovascular system to a greater degree than young normotensives, which implying aging more pronounced reductions in cardiac and vascular compliance. SHS exposure as an acute threat paradigm for the cardiovascular system. We used exposure to SHS exposure to divide from aging-induced cardiovascular system. According to our initial results, we had made sure left ventricular hypertrophy will be induced during aging and exposure to SHS of young and aging rats. LV chamber enlargement and strong cardiac remodeling in young adult SHS exposure, aging and aging SHS exposure. Whereas pathological left ventricular hypertrophy is commonly associated with up-regulation of fetal genes, ANP and BNP. In this study we also observe their expression elevated. However, SHS exposure is a key risk factor for pathological hypertrophy associated with various cardiovascular disease risk factors. Cardiac health of aging exposure to SHS is our main interesting. We further investigate molecular signaling mechanisms associated with the development of pathological hypertrophy including IGF-II/IGF-IIR/Gαq/calcineurin/NFAT, IL-6/MEK-5/ERK-5, MEK1-ERK1/2-GATA4 and JAK/STAT signaling pathways. Over the past few years, we determined that IGF-II/IGF-IIR/Gαq/calcineurin/NFAT, IL-6/MEK-5/ERK5, JAK/STAT and MEK1-ERK1/2-GATA4 signaling pathways were induced during pathological hypertrophy. From our results we found young SHS exposure induced left ventricular hypertrophy via JAK1/STAT1 activation. However, both concentric and eccentric left ventricular hypertrophies were occurred in aging and aging SHS exposure. One possibility is that ageing is highly sensitive to low level of SHS exposure and even exposure under one hour per day, has already increased and accumulated its toxicity. On the other hand, in some way cross-talk between calcineurin/NFAT and MEK1/ERK1/2 signaling induces LVH growth response. Aging simulate activate many intracellular signals dramatically affects the orchestration of LVH response and effectively augments heart enlargement. Eventually, the calcineurin/NFAT, MEK5/ERK5, JAK2/STAT3 dependent mechanisms are interacted and compensated (40). It is also possible that new NFAT complex occurred which may not only depend on the degree of calcineurin activation. We were speculating that LV concentric and eccentric hypertrophy both occurred in aging and aged SHS exposure, however, physiological hypertrophy was presented in young SHS exposure. It should be noted that aging has more exacerbated than SHS exposure. Nevertheless, this is because of calcineurin/NFAT and MEK1-ERK1/2 through transcriptional mediators, NFAT and GATA4, direct or indirect interactions regulate cardiac hypertrophy in aging and aged SHS exposure. Indeed, ERK1/2 activation induced concentric hypertrophy, and cross talk with calcineurin/NFAT pathway resulted in eccentric hypertrophy. In addition, the JAK2/STAT3 and calcineurin/NFAT signaling pathways might coregulate cardiomyocyte hypertrophy as well. The JAK1/STAT1 protein expression levels were only enhanced by SHS exposure in young rats. Indeed, accumulated evidence shows SHS exposure in

different age has different level damage in left ventricular. However, epidemiological evidence indicates exposure to SHS is an increase with age in the incidence of CVD. High-dose secondhand smoke exposure definitely will be harmful to cardiovascular function in healthy adults. Therefore, our evidences further provide a theoretical paradigm by which low-dose SHS exposure is sufficient to harm and accelerate aging left ventricular transition from hypertrophy to heart failure. Extensive evidence SHS exposure toxicity will compromise with young age healthy. Although aging has been constructed as physiological adaption response, but not pathological response. Nevertheless, the aging induced cardiac concentric or eccentric pathological hypertrophy was highly augmented by SHS exposure was detected in this report.

Physiological Aging Heart

Aging is a complex process which is difficult to define. Physiological aging is generally defined to be a decline body function take place in the absence of any discernible disease process. The process of aging refers to divisions into the young old (65-74 years old), the middle old (75-84 years old), and the oldest old (85+ years old). It is mostly acknowledged that healthy aging of the cardiovascular system is distinct from the increasing incidence and cardiovascular disease with advancing age. Therefore, aging can be divided into two types: physiological and pathological aging. The most well recognized risk factor for many chronic diseases in physiological aging. Interactions between the aging process and the aged-related disease has not been seriously addressed or systematically explained. Aging is an inevitable process of life. Cardiac aging is defined as the structural changes and functional declines with the onset of disease or degradation, but in the absence of environmental factors major cardiovascular risks such as smoking, hypertension, diabetes, and hypercholesterolemia. Aging-associated degeneration is a major risk factor for cardiovascular disease. This physiological aging changes of cardiac included left ventricular hypertrophy, increased cardiac fibrosis and valvular degeneration. However, the high prevalence of hypertension and ischaemic heart disease makes distinction between normal aging changes and the effects of underlying cardiovascular disease processes difficult. Left ventricular aging is a complex process which is still not well understood. Thus, cardiovascular disease is a major risk factor for old age cause of death. In this study, we focus on aging-dependently physiological cardiovascular outcome. We discuss whether physiological aging of LV is also associated with cardiovascular disease, hypertrophy and failure. Moreover, we determined aging-related cardiac diseases is associated with numerous molecular and biochemical changes in the heart. Age changes affect cardiac-related protein function and cardiac morphology result in alterations of cell death and survival. LVH is an initial adaptive response in order to protect heart functions. During LVH development, there are a lot of compensatory mechanisms to increased cardiac work-load and stimulation left ventricular sustains. Become progressively disorganized and degraded with age occurring as consequence of physiological aging. Aging process can be described as a progressive functions decline that lead to the accumulation of errors that damage repair systems and compromise stem cell function. These can be caused physical, mental, and reproductive capacity decline through genetic and epigenetic mechanisms result to the cell dysfunction. Because there is a decline in food intake will make the lifespan shorter. This physiological change in aging will take place older man at risk of developing pathological weight loss, when they develop diseases states. This phenomena has been described as the physiological anorexia of aging and may be due to altered hedonic qualities of food, early satiation because of changes in adaptive relaxation and an excess satiating effect of cholecystokinin. Physiological aging related diseases such as sarcopenia and osteopenia are associated with reduced functional capacity, increased risk of falls, and loss of independence. Although aging is inevitable, with advancing age, even in healthy adults, eventually, the perform certain physical task capacity reduced results in increased incidence of function disability. Physiological aging changes are not caused by disease or environmental influences. Age-associated deterioration is the interaction between genes and environment factors that usually plays the major role in physiological functions rather than genes by itself or environment by itself (Figure 1). Understanding the basic physiological aging processes can decide making sustain quality of life in an aging. Aging is an unavoidable physiological response, which is an inevitable process, random and passive decline in function, and leading to loss of homeostasis over time. The physiologic changes of the aging cardiac includes left ventricular hypertrophy, increased cardiac fibrosis and valvular degeneration. Cardiovascular disease is a major risk factor for aging cause of death. Physiological aging is age-related decline which lead to function decline, however, pathological aging is aging-related disease which is aging results in diseases (Figure 2). Diseases that do not occur until, or increase in frequency at advanced ages are called age-associated diseases. Indeed, age-associated disease underlies much of the physiological deterioration of old age. The most well recognized risk factor for many chronic diseases in physiological aging. Interactions between the aging process and the aged-related disease has not been seriously addressed or systematically explained. Aging is an inevitable process of life. Become progressively disorganized and degraded with age occurring as a consequence of physiological aging. Aging process can be described as a progressive function decline that lead to the accumulation of errors that damage repair systems and compromise stem cell function. These can be caused physical, mental, and reproductive capacity decline through genetic and epigenetic mechanisms result to the cell dysfunction. Because there is a decline in food intake will make the lifespan shorter. This physiologic change in aging will take place older man at risk of developing pathological weight loss, when they develop diseases states. Physiological aging related diseases such as sarcopenia and osteopenia are associated with reduced functional capacity, increased risk of falls, and loss of independence. Although aging is inevitable, with advancing age, even in healthy adults, eventually, the perform certain physical task capacity reduced results in increased incidence of function disability. Physiological aging changes are not caused by disease or environmental influences. Age-associated deterioration is the interaction between genes and environment factors that usually

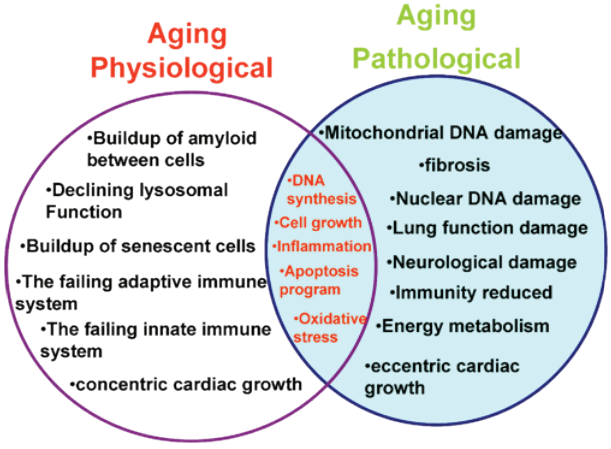

Figure 2: Distinctions may be made between "physiological aging" and "pathological aging". Understanding the basic physiological aging processes can decide sustain quality of life in an aging. Aging is strongly correlated with a higher incidence of disease disorders such as cancers, diabetes, Parkinson's disease, Alzheimer's disease and dementia. Although to analyze the normal ageing process, free of the underlying effects of added diseases, dietary and environmental factors is very difficult, the fact that apoptosis is strictly associated with this process, in eliminating redundant, damaged or infected cells is generally accepted. In any case, the complex phenomenon of aging in cells and tissues is associated with number of environment peculiar morphological, histological, genetics, epigenetics and biochemical changes.

plays the major role in physiological functions rather than genes by itself or environment by itself. Distinctions may be made between "physiological aging" and "pathological aging" (Figure 2). Understanding the basic physiological aging processes can decide making sustain quality of life in an aging. Advanced age is always accompanied by a general decline in organ function even in the absence of overt coexisting disease that do not occur until, or increase in frequency at, advanced ages are called age-associated diseases. Indeed, age-associated disease underlies much of the physiological deterioration of old age. Apoptosis is a recognized mechanism for the elimination of redundant cells in the pathogenesis of cardiac disorders in the elderly. Cardiac aging generates a complex phenotype. Numerous molecular and biochemical changes in the heart is associated with aged-related cardiac disease. These changes affect protein function and cardiac morphology resulting in alterations in cell death and survival. The biochemical changes also affect the expression levels of mitochondrial membrane free radical changes. In aging, apoptosis is upregulated in various cell tissues in a different manner. In myocardial tissue, fundamental processes have been evidenced, independently of the presence of cardiovascular disease, which contribute to maintain the homeostatic state to ensure the normal function. Aging of the heart implies a reduced number of myocytes and of specialized conduction tissue cells, which are not replaced, because of the inability of adult cell to divide. In addition, reduction in Ca++ transport across membranes, lower capillary density and decreased sensitivity of the cardiovascular system to βadrenergic stimulation characterize this physiological state. Among the molecular mechanisms regulating apoptosis, a role for the pathway PI-3-kinase/AKT-1 has been suggested. PI-3-kinase plays a key role in many cellular processes such as differentiation, mitogenic signaling, cytoskeletal remodeling, vesicular traffic, apoptosis. One of the targets of its specific product PI3, 4, 5P3, is represented by the protein serine/threonine kinase AKT/PKB. PI-3-kinase/AKT1 is reported to deliver a survival signal, giving to the cell the chance to recover from some damage. This pathway seems to regulate the activation of the Bcl-2 family members or/and inactivation of the CED3/ICE family of proteases, as elsewhere reported. The Bcl-2 protein family plays a central role in the regulation of apoptosis. These proteins take part with antiapoptotic (Bcl-2, Bcl-xl) and pro-apoptotic members (Bax, Bad, Bak), whose reciprocal balance is fundamental in determining cell fate. The final execution phase, when it occurs, results in the activation of a family of proteases, the caspases, which participate in a cascade of events leading to the cleavage of a set of proteins, causing disassembly of the cell. Apoptosis, or programmed cell death, is a recognized mechanism for the elimination of redundant cells in the pathogenesis of human cardiac disorders in the elderly. Cardiac TGF-I triggers intracellular signaling cascades that are involved in modulating and facilitating growth and survival and promotes apoptosis. In addition, the death-receptor-induced apoptotic pathway which is initiated by death-agonists and involves the Fas ligand, (Fas-FADD-caspase 8-Bid) is reportedly involved in the pathogenesis of cardiac disease. Mitochondria may play an important role in apoptosis by releasing cytochrome c, bad, bcl2 and caspase 9. However, caspase 3 apoptosis signaling mediates both mitochondria-dependent and death-receptor-dependent apoptotic pathways. In cardiomyocytes, insulin-like growth factor (IGF-I) activates PI3K (phosphatidylinositol-3-kinase)/Akt (PKB, protein kinase B) signaling through IGF-IR and is considered to play a role in preventing myocyte apoptosis. The important role of IGF-I and IGF-IR in growth and development and their involvement in the prevention of cell apoptosis have been elucidated. In cardiomyocytes, PI3k activity is required for IGF-I and its receptor (IGF-IR), and PI3K-generated phospholipids regulate AKT activity by direct binding of phosphoinositide to the PH domain. In aging, apoptosis is upregulated in various cell tissues in a different manner.

Pathological Aging Heart

Aging is a physiology unavoidable process leading to random and passive loss of homeostasis in function. Over time involving progressive impairment of normal heart function due to an increasing vulnerability, which reduces the ability of survive. However, it is not clear pathological condition in aging exposure to SHS. Aging is considered as a major risk factor cardiovascular disease. Various age-associated changes in the cardiovascular system may lead to pathological outcomes including cardiomyocyte death, arterial stiffening, myocardial hypertrophy, and desensitization of β-adrenergic signaling specifically by alterations in structure and function of the heart and vasculature that will ultimately affect cardiovascular performance. Cardiac remodeling during aging includes cardiomyocyte loss, reactive hypertrophy of the remaining cells and increased interstitial tissues. These changes may result in a decline in the biological and physiological functions of the heart. It has been suggested that the aging-induced cardiac changes render the heart more susceptible to ischemic damage. Observational studies have reported that Intrinsic cardiac aging is a human physiologic change which has the slowly progressive structural changes and functional declines with age, however, which in the absence of major cardiovascular risks. One of the major difficulties encountered in the study of the effects of age on the cardiovascular system is the differentiation of the aging process itself from the presence of specific disease states. Atherosclerosis, diabetes, and ischemic heart disease are common events in humans, and the severity of these pathological conditions increases with age. Moreover, remodeling of the heart that occurs with advancing age may be in response to left ventricle hypertrophy and increased wall stress and observed with early heart failure and increased fibrosis. Therefore, the normal old-age heart changes which can mimic cardiac disease. Age-related diseases were also accompanied with an augmentation of fibrotic area and muscle fiber architectural rearrangements in the ventricular myocardium. Remodeling of the aging left ventricle typically involves a large net loss of active cardiac myocytes, reactive left ventricle of the remaining cells, and increased accumulation of connective tissue. At the same time, the mechanism responsible for the left ventricular fibrosis in the senescent is unclear. These myocardial mechanical properties will result from alternation of collagen. Myocardial collagen is affected by aging process. The Matrix Metaloproteinases (MMP2 and MMP9) are responsible for extracellular collagen degradation and remodeling. The roles of TGF-β1 and MMPs (MMP2 and MMP9) in left ventricular remodeling are intertwined. Both proteins are complex for fibrosis, and both concentrations were elevated. However, the activities of MMPs are regulated by TIMPs. Moreover, TGF-β1 is induction through connective tissue growth factor to up-regulate pro-fibrotic proteins. Aging is a human inevitable adaptive response to exhausted cells, while others regard it as a process that starts at conception and continues until death. Biologists consider aging to be a human physiologic change which has the slowly progressive structural changes and loss in body function with age. The age- and disease-dependent alterations to total MMP activity are changes to myocardial collagen content occurring in cardiac fibrosis. In this report we make separate aging-related changes from those related to disease, and to outline their significance for cardiac remodeling. In the aging heart, there is transition of fibroblasts to myofibroblasts and accumulation of extracellular matrix protein in the interstitium. The histopathologic images show fibrotic remodeling of the left ventricular in aging and SHS exposure. Fibrosis occurs in most injuries and results from changes in the balance between synthesis and degradation of extracellular matrix components. Transforming growth factor-β1 (TGF-β1) is a biologically active peptide that is present in normal cells, including fibroblasts. According to the result, it has been demonstrated that TGF-β1 and CTGF stimulate the expression of collagen and its appearance in the extracellular matrix in aging and SHS exposure rats. In addition, FGF-2 and UPA may contribute to fibrosis by collagen accumulation. However, overexpression of urokinase causes accelerated atherosclerosis, coronary artery occlusions and premature death. It is possible that by simultaneously targeting multiple pathogenic pathway. On the other hand, the MMPs are an endogenous enzyme system responsible for extracellular collagen degradation and remodeling. With exposure to secondhand smoke exposure, an enhanced extracellular matrix degradation by increasing the expression of MMP2 and MMP9, inhibiting TIMPs expression. At this time, elevated expression of MMP2 and MMP9

during fibrogenesis permits an immediate metalloproteinase reactivity as soon as TIMP-1, TIMP-2, TIMP-3 and TIMP-4 levels declined. With aging-dependent changes in cardiac remodeling, dysregulation of MMP2 and MMP9 are believed to contribute to fibrosis and aging. These observations suggest that depression of the degradative pathway is partly responsible for age-associated fibrosis. However, MMP 2 and MMP9 activity are decreased with aging and increased with exposure to SHS exposure. Elevation of TIMPs (TIMP-1, TIMP-2, TIMP-3 and TIMP-4) we observed with aging was indeed consistent with upstream suppression of active and ECM fraction forms MMP2 and MMP9. Interestingly, these results we observed on aging exposure to SHS exposure. Specially, TIMP-4 expression in the aging exposure to SHS, failing myocardium could lead to enhanced ECM remodeling through loss of MMP2 leading to cardiac dysfunction. Summary, TGFβ1 is a potent stimulator of TIMPs including TIMP-1, TIMP-2, TIMP-3 and TIMP-4 and a potent contributor to fibrosis in the aging LV. Together, evidence that aging suppresses MMPs (MMP9 and MMP2) production in the left ventricular. Human cardiac aging generates a complex phenotype. Experimental evidence in animal models indicate attenuation in cardioprotective pathways with aging, yet limit myocardial dysfunction information in the aging. It is available regarding aging-related changes also in the human left ventricle heart. Some of the age-associated changes in the heart can be reversed, at least partially, by exercise or specific drugs. It remains, however, unclear whether aging would result in any definite disease. The changes of the heart throughout life are therefore the result of maturational changes beyond sexual maturity and the age changes, which controlled hypertrophy of myocytes and hyperplasia of capillary endothelial cell and interstitial fibroblasts.

Successful aging

Successful aging is the accumulation of the gradual structural changes in persons over time, but are not due to disease or disability-free life well through their later years, and that eventually lead to death. Successful aging is an important part of human societies refers to a multidimensional process of physical and cognitive capacity reflecting the biological changes occurs, but also reflecting cultural and societal conventions, even late in life, potential exists for physical, mental, and social growth and development. We can define successful aging consists low probability of disease or disability over the age of 75 as rated by a physician, and have subjective health assessment, good mental health, and high cognitive and physical function capacity. Active engagement with life, friendship, social contacts, hobbies, community service activities. Life span extension can be established by support system of family, friends, and health care providers, on the other hand, together with focus on good nutrition and lifestyle habits and good stress management, can prevent disease and lessen the impact of chronic conditions. Lifespan shortened can occur as the result of genetic alterations, thus, increase DNA repair, reduce oxidative damage or reduced cell suicide due to DNA damage can make life span longer. Health aging is the gradual bodily structural changes that occur with time-dependent, but that are not due to disease or other gross accident, and that eventually lead to death. After the normal transition time aging, an individual is more prone to have problems with the various body functions and develop disease. Thus, ageing-related changes may lead to any number of chronic or fetal disease such as Alzheimer, cancer, diabetes and heart disease (Figure 2). Many problems can due to aging-related changes. The cardiovascular and digestive are particularly affected. Cardiac aging is a human physiological changes which has the slowly progressive structural changes and functional declines with age, however, which have to in the absence of major cardiovascular risks such as high blood pressure. Successful aging is the accumulation of the gradual structural changes in a persons over time, but are not due to disease or disability-free life well through their later years, and that eventually lead to death. Successful aging is an important part of human societies refers to a multidimensional process of physical and cognitive capacity reflecting the biological changes occurs, but also reflecting cultural and societal conventions, even late in life, potential exists for physical, mental, and social growth and development. Successful aging consists of three components: (a) Low probability of disease or disability over the age of 75 as rated by a physician. (b) Good subjective health assessment, good mental health, and high cognitive and physical function capacity. (c) Active engagement with life, friendship, social contacts, hobbies, community service activities.

Age-related cardiac fibrosis

The interstitial collagen matrix is an important component of the myocardium, which surrounds and supports cardiac myocytes and the coronary microcirculation. The interstitial collagen also maintains the myocytes alignment, the myocyte–capillary relationship, and the heart architecture throughout the cardiac cycle. Therefore, the form and distribution of the connective tissue of the heart is such that it may play an important role in the elastic properties and viscous properties of the left ventricle. The major types of collagen present in the interstitium of myocardium are I, III and V, with type I predominating. In non-human primate myocardium, for example, the distribution of collagen types is as follows, 85% type I; 11% type III and 3% type V. In the myocardium, fibers which surround large bundles of myocytes and individual myocytes appear to be a copolymerization of the I and III collagen molecules. Collagen is the only protein in the organism showing definite age changes. A relationship with the general process of aging has, therefore, been assumed. Physicochemical changes in the chemical and thermic contraction have been demonstrated in collagen fibers of different ages. Moreover, biochemical changes in the tissues such as a decrease in the content of extractable collagen show a relationship with increasing age, and the total collagen content in certain tissues has been found to increase with age. In order to understand the changes in the human myocardial tissue in disease, knowledge of their detailed structure in the normal state is required. However, there have been few studies on the aging of collagen in the human heart. The aim of the present investigation was to determine the types of collagen, to measure the collagen content and the collagen fibril diameters of the left ventricle of the human heart and to observe any differences between young and aged. Myocardial connective tissue plays an important role in defining and preserving normal myocardial architecture and function. Excess deposition of collagen in extracellular matrix can lead to increased myocardial stiffness and subsequently to cardiac hypertrophy and LV dysfunction. These pathological changes increase the risk of Heart Failure (HF) and provide an anatomic substrate for life-threatening cardiac arrhythmias. Type I and III collagens are the major fibrillar collagens in both normal and diseased myocardium. Both are synthesized as procollagen with a small amino terminal and a larger carboxy terminal pro-peptide. Serum markers of fibrosis reflecting collagen synthesis include carboxy-terminal pro-peptide of type I procollagen (PIP) and amino-terminal Pro-Peptide of type III procollagen (PIIINP), and degradation markers include carboxy-terminal telopeptide of collagen type I (CITP). Elevations in these fibrosis markers have been shown to reflect intramyocardial collagen turnover. The collagen concentration and the intermolecular cross-linking of collagen increase with age. Activated MMPs degrade the collagen network and subsequently result in the loss of structural support, distortion of tissue architecture, wall thinning, and infarct expansion. Collagen is the only protein in the organism showing definit age changes. Collagen in many organs qualitatively and quantitatively changes with age. A relationship with the general process of aging has been assumed. An increase in crosslinking of the collagen macromolecules occurs with aging. The total collagen content in many tissues has been found to increase with age, condition referred to as fibrosis. Myocardial collagen is also affected by the normal aging process. There are provide consistent evidence of an increase in myocardial collagen associated with aging. We also observed that there were greater areas of fibrosis in the hearts of the old rats when compared with those of young rats. It is well established that the aging process of the heart is characterized by a loss of myocytes. These reductions occur because myocytes are post-mitotic cells and are not replaced, as they die. The loss of myocytes could explain the accumulation of collagen in the walls of the ventricles. Another mechanism for collagen accumulation with age could be

inhibition of collagen degradation. The collagen degradation process in the myocardium by normal aging which a possible explanation is that it is related to cardiac pressure overload.

Sarcopenia in Older People

Sarcopenia is one of the leading causes of reduced skeletal muscle mass and strength in order adults. Inflammation- aging with aging is known to be a major contributor to sarcopenia. Therefore, sarcopenia has been defined as the loss of skeletal muscle mass and strength in the older age. This group proposed that sarcopenia is diagnosed based on a low whole-body or appendicular fat-free mass in combination with poor physical functioning. Sarcopenia is a newly recognized geriatric syndrome by age-related decline of skeletal muscle plus low muscle strength and/or physical performance through a combined approach of muscle mass and muscle quality. This is an importance of sarcopenia in the health care for older people. Sarcopenia starts at approximately 40 years of age and there is an estimated muscle mass loss of about 3~8% per decade, stretching process speeds up until the age of 70 years; after that age, a 15% loss ensues per decade. Sarcopenia has since been defined as the loss of skeletal muscle mass and strength that occurs with advancing age. With aging, sarcopenia has been defined as a syndrome characterized by progressive and generalized decline in skeletal muscle mass and strength, increasing the risk of adverse outcomes such as physical disability, poor quality of life, and death. However, a widely accepted definition of sarcopenia suitable for use in research and clinical practice is still lacking. Sarcopenia increases the risk of falls and fractures and susceptibility to injuries and can be the cause of functional dependence and disability in the elderly population. However, on average, by 20-40% for both men and women in proximal and distal muscles. Thus, defining sarcopenia only in terms of muscle mass is too narrow and may be of limited clinical value that becomes more common in people over the age of 50. After middle age, adults lose 3% of their muscle strength every year, on average, to perform many routine activities. These factors contribute to sarcopenia and to the characteristic skeletal muscle atrophy and weakness. Sarcopenia also shortens life expectancy in those it affects, compared to individuals with normal muscle strength. Aging sarcopenia is caused by an imbalance between signals for muscle cell growth and signals for teardown. Cell growth processes are called “anabolism,” and cell teardown processes are called “catabolism”. For example, growth hormones act with protein-destroying enzymes to keep muscle steady through a cycle of growth, stress or injury, destruction and then healing. However, during aging, your body becomes resistant to the growth signals, tipping the balance toward catabolism and muscle loss.

Sarcopenic obesity in older adult Rheumatoid Arthritis (RA) patients

RA status was significantly associated with greater odds of sarcopenia, overfat, and sarcopenic obesity in women, but not in men. Among older adult RA characteristics, increasing joint deformity, disability scores, C-reactive protein levels, rheumatoid factor seropositivity, and a lack of current treatment with disease-modifying antirheumatic drugs were significantly associated with abnormal body composition. During this time, reduced lean mass, at its extreme termed sarcopenia and excess body fatness are predictors of poor health outcomes in the general population. Sarcopenic obesity is the combination of muscle loss and fat mass gain, loss of lean mass may lead to weakness, disability, and metabolic abnormalities. Sarcopenic obesity is at its extreme referred to as theorized compound these individual risks. Overall prevalence of sarcopenia was 35.4% in women and 75.5% in men, which increased with age. Prevalence of obesity was 60.8% in women and 54.4% in men. Sarcopenic obesity prevalence was 18.1% in women and 42.9% in men. Older women with sarcopenia have an increased all-cause mortality risk independent of obesity. Sarcopenic obesity with rheumatoid arthritis and aging, loss of muscle mass as a primary event, and this loss is a major contributor to fat gain, which in turn reinforces the muscle loss. Markedly elevated TNF and IL-1 production in RA, and the various etiologic factors of sarcopenia in aging all lead to loss of muscle. With the increase in fat mass, leptin and TNF secretion are increased, and both lead to insulin resistance, which reduces the normal anabolic effect of insulin on amino acid transport in muscle. In addition, there is some evidence that leptin reduces growth hormone secretion, suppressing another major anabolic stimulus. In addition, higher TNF levels may exert direct catabolic effects on muscle. Obesity in the older adult is associated with poorer performance and strength parameters. The purpose of this study was to determine the underlying mechanisms of muscle wasting in sarcopenia obesity patients with rheumatoid arthritis (RA) in the elderly. The abnormalities in body composition and abdominal fat that occur in rheumatoid arthritis (RA) are associated with aging related presence of skeletal muscle dysfunction. Histone Deacetylases (HDACs) have been implicated in muscle atrophy and dysfunction due to denervation, muscular dystrophy, and disuse, and HDACs play key roles of HDACs in muscle atrophy and the potential of HDAC inhibitors for the treatment of sarcopenia in regulating metabolism in skeletal muscle. Several HDAC isoforms are potential targets for intervention in sarcopenia. Inhibition of HDAC1 prevents muscle atrophy due to nutrient deprivation. HDAC3 regulates metabolism in skeletal muscle and may inhibit oxidative metabolism during aging. HDAC4 and HDAC5 have been implicated in muscle atrophy due to denervation, a process implicated in sarcopenia. HDAC inhibitors are already in use in the clinic, and there is promise in targeting HDACs for the treatment of sarcopenia.

Nicotine toxicity effect on aging-related cardiovascular disease and cancer

Nicotine is highly addictive to cardiovascular disease. Nicotine is insufficient as a carcinogen, it’s functions as a tumor promoter on purpose. It follows that nicotine is only associated with cardiovascular disease in old humans. Nicotine promotes cancer growth, angiogenesis and neovascularization. However, nicotine alone is generally accepted as a tumor promoter, but not a tumor initiator in carcinogenesis. Nicotine constitutes approximately 0.6~3.0% of the dry weight of tobacco. Like anything that enters the body, nicotine is also metabolized. Therefore, any activity that increases your metabolic rate can help speed up the clearance of nicotine. Exercise is a good way to increase the rate of metabolism. Exercise improves heart rate and increases the rate of metabolism and burning of heat. For people who have many years of smoking, it is important to start exercising. Make sure to drink plenty of water because nicotine is soluble in water, so drinking water helps to excrete the substance through the urine. Vitamin A is also helpful in removing nicotine from the body because it also has the effect of speeding up the metabolism. Because nicotine tends to destroy vitamin C in the body, it is important to supplement it after quitting smoking. Nicotine is a nitrogen-containing chemical, an alkaloid, which is made of tobacco plant. Nicotine is also produced synthetically. Nicotine acts as both a sedative and a stimulant. Many people smoke and many people continue their craving for a lifetime. Because nicotine is one of the most addictive substances, one of the important ways to get rid of this bad habit is to get rid of nicotine in your body. Knowing how long it takes and how to speed it up can help you quit smoking sooner. Nicotine enters the body through smoking. In addition to smokers, others inhale nicotine through secondhand smoke. In general, about 1-2 mg of nicotine is taken from each cigarette. After nicotine inhales the lungs, it enters the bloodstream and is distributed throughout the body. We all know that nicotine is a toxic substance and is metabolized by the kidneys. Nicotine dissolves in water and excretes through the liver and urine. Most of the intake of nicotine smoke will soon be excreted through the urine. This is also one of the reasons that easily lead to excessive smoking, because smokers need to continue to be satisfied. After nicotine enters the bloodstream, it circulates in the body. A cigarette nicotine completely discharged from the body usually takes 6-8 hours. However, nicotine is present more in the heavily smoker. After years of smoking, nicotine deposits on fat cells and spreads throughout the body. Once quit-most of the body’s nicotine is metabolized and excreted in 48-72 hours. However, since nicotine adheres to fat cells and other body parts, it takes longer to

remove it completely. In addition, cotinine, a by-product of burning nicotine, resides in the body for 30 days. When inhaled cigarettes, nicotine will directly into the lungs. Afterwards, oxygenated blood is sent to the brain through the heart. In less than ten seconds, a concentrated dose of nicotine is delivered to the brain's blood vessels and produces a nicotine effect. Smoking will lead to lung cancer is an indisputable fact. Tobacco combustion is a very complex chemical reaction process, because of the inability to control these reaction processes, naturally, can't control the production of harmful ingredients. Nicotine is a key factor in smoking addiction. Nicotine is not carcinogen, but it induced cardiovascular diseases. Because of there is no evidence that nicotine itself provokes cancer. Nicotine binds to nicotinic-acetylcholine receptors (α7nAchR) or EGF receptors, leading to activation of protein kinase B, protein kinase A and other factors. This leads to downstream effects, such as decreased apoptosis, increased cell proliferation and transformation. Although EGFR tyrosine kinase inhibitor leads to a great treatment advance of cardiovascular diseases in old man, only a subgroup with EGFR activating mutation benefits from it. During the tobacco curing and smoking process, nicotine can be converted to mainly 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) through nitrosylation. In Secondhand smoke (SHS) exposure, NNK-induced proliferation appears to involve activation of the α7nAChR, MEK, protein kinase C (PKC), and c-myc. Repeated exposure of Secondhand smoke (SHS) exposure to nicotine increases collagen breakdown and transmigration in conjunction with increased tumor growth, vascularity, and resistance to chemotherapy. Nicotine increases cardiovascular diseases and lung cancer cells through activation of the α7nAChR, c-Src and PKCiota. It is suggested that the effects of NNK appear to be mostly dependent upon the α7nAChR. Nicotine binds to nicotinic-acetylcholine receptors (α7nAchR), EGFR and other receptors, leading to activation of Akt, PI3K and other factors. This leads to downregulation effects of cell growth as well as decreased apoptosis, increased cell proliferation and transformation. Nicotine also stimulates tumor angiogenesis and cardiovascular disease, which is also mediated through α7nAchR, possibly involving endothelial production of nitric oxide (NO), prostacyclin and vascular endothelial growth factor. Nicotine might have tumor-promoting or co-carcinogenic activity. Nitric oxide (NO) is synthesized by three key enzymes of nitric oxide synthase (NOS) from the amino acid L-arginine. Inducible nitric oxide synthase (iNOS) is one of three key enzymes generating nitric oxide (NO). Nitric oxide (NO) plays an important role in the physiological and pathophysiological conditions. Neuronal NOS (NOS1, nNOS) and endothelial NOS (NOS3, eNOS) are constitutive calcium-dependent forms of the enzyme that regulate neural and vascular function respectively. The third isoform (iNOS, NOS2), is calcium-independent and is inducible. iNOS is the synthase isoform most commonly associated with malignant disease. Nevertheless, the role of iNOS during tumor development is highly complex, and incompletely understood. iNOS activity has been demonstrated in various cell types including macrophages, chondrocytes, Kupffer cells, hepatocytes, neutrophils, pulmonary epithelium, colonic epithelium, vasculature, and neoplastic diseases. Regulation of NO production via iNOS necessarily occurs during transcription and translation. Once active, iNOS synthesizes large amounts of NO until substrate depletion. Most of Non-small cell lung cancer (NSCLC) are unsuitable for chemotherapy remains the cornerstone of treatment for advanced cardiovascular diseases. Platinum-based doublet chemotherapy remains the mainstay for advanced NSCLC. Nicotine binds to nicotinic-acetylcholine receptors (α7nAchR) leading to activation of the Akt. Nicotine can stimulate angiogenesis tumor growth and cardiovascular disease which is also mediated through α7nAchR, possibly active involving NO and Endothelial Growth Factor (EGFR). Some report indicate nicotine might have tumor-promoting or co-carcinogenic activity. Nicotine is the leading risk factor of lung cancer. Several clinical studies suggest that continuation of smoking during therapy of tobacco-related cancers is associated with lower response rates to chemotherapy and/or radiotherapy, and even with decreased survival. Although nicotine is not a carcinogen, it may influence cancer development and progression or effectiveness of anti-cancer therapy. Several trials have evaluated the influence of nicotine on lung cancer cells. The best known mechanism by which nicotine impacts cancer biology involves suppression of apoptosis induced by certain drugs or radiation, promotion of proliferation, angiogenesis, invasion and migration of cancer cells. This effect is mainly mediated by membranous nicotinic acetylcholine receptors whose stimulation leads to sustained activation of such intracellular pathways as PI3K/Akt/mTOR, RAS/RAF/MEK/ERK and JAK/STAT, induction of NF-κB activity, enhanced transcription of mitogenic promoters, inhibition of the mitochondrial death pathway or stimulation of pro-angiogenic factors. These mechanisms underlying nicotine's influence on biology of lung cancer cells and the effectiveness of anti-cancer therapy. Smoking is a major cause of human lung cancer and cardiovascular disease. However, the mechanism by which nicotine induces cardiovascular disease to the cancer remains obscure, although in nicotine carcinogenesis, promotion co-carcinogenesis may have crucial roles. Nicotine exhibits co-carcinogenic and promoting activities in tumour production and malignant transformation. Nicotine promoted NSCLC lung cancer in all patients, the role of nicotine underlying mechanisms through α7nAChR nicotine receptor signaling in lung cancer in old man is still unknow. Primary results showed nicotine promoted α7nAChR, NOS2, EGFR and cell cycle related protein, Cyclin D1/pRb and Cyclin E/E2F increases. Therefore, we suggest nicotine promoted cell cycle actives through receptor α7nAChR or EGFR induced. In the present study, we also want to know nicotine related into cell cytoplasm and nuclear regulation. Low concentration level of nicotine increases migration and invasion of lung cancer cells through activation of the α7nAChR, c-Src, and PKC. Nicotine binds to nicotinic-acetylcholine receptors (α7nAchR), EGFR and other receptors, leading to activation of the Akt, PI3K and other factors. On the other hand, nicotine directly regulated NOS2 expression in a α7nAchR dependent manner. Its activation resulted in regression of tumor cell growth and inactivation of cellular apoptosis via DNA damage to α7nAchR and СКЦ α activation in lung cancer cells in the elderly. A time-dependent nicotine treatment induced NOS2 expression and p-Akt increases. Because frequent loss of function of the NOS2 protein by nitrosylation was reported in lung cancer, the nicotine-mediated induction of NOS2 may provide one of its links to α7nAchR. Smoker or nicotine exposure may affect either cardiovascular disease or cancer cells. Furthermore, cell membrane receptor proteins, α7nAChR and EGFR, related-nicotine effects. This effects maybe is time-dependent and dose-dependent to regulate NSCLC cell growth. That is our anticipated results and want to resolution. Intricately, we can use these findings to help new drugs development.

CONCLUSIONS

Aging is a physiological process which is from birth to aging the heart undergoes functional changes and which reflect biochemical and ultrastructural modifications, involving progressive impairment of normal functions. Aging of the heart is associated with number of characteristic morphological, histological and biochemical changes. Because the contribution of these variables to the alterations of the aged myocardium cannot easily be separated from the aging phenomenon alone, the changes of the heart throughout life are therefore the result of multifactorial events in which aging plays an important but indistinguishable role.

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CONFLICT OF INTEREST STATEMENT

None.

ABBREVIATIONS

SHS, Secondhand smoke; LVH, Left ventricular hypertrophy; CHD, coronary heart disease; CVDs, cardiovascular diseases; ECM, extracellular matrix. NSCLC, Non-small cell lung cancer.

BIBLIOGRAPHY

1. Eisner M.D., J. Balmes, P.P. Katz, L. Trupin, E.H. Yelin, P.D. Blanc. 2005. Lifetime environmental tobacco smoke exposure and the risk of chronic obstructive pulmonary disease. Environ. Health 4:7.
2. Oberg, M., M.S. Jaakkola, A. Woodward, A. Peruga, A. Prüss-Ustün. 2011. Worldwide burden of disease from exposure to second-hand smoke: a retrospective analysis of data from 192 countries. Lancet 377:139-146.
3. Thun, M.J., B.D. Carter, D. Feskanich, N.D. Freedman, R. Prentice, A.D. Lopez, P. Hartge, S. M. Gapstur. 2013. 50-year trends in smoking-related mortality in the United States. N Engl J Med. 368:351-364.
4. U.S. Department of Health and Human Services. 2014. The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta, GA. Google Scholar
5. World Health Organization. 2016. Tobacco –fact sheet. Available at: http://www.who.int/mediacentre/factsheets/fs339/en/. Accessed: June 15, 2017.Google Scholar
6. Schönherr, E. 1928. Contribution to the statistical and clinical features of lung tumors. Z. Krebsforsch. 27: 436-450.
7. Sullivan, S.D., S.D. Ramsey, T.A. Lee. 2000. The economic burden of COPD. Chest 117(2Suppl.): 5S-9S.
8. Behan, D.F., M.P. Eriksen, Y. Lin. 2005. Economic Effects of Environmental Tobacco Smoke. Society of Actuaries, Schaumburg, IL. Available at: https://www.soa.org/research-reports/2000-2006/research-economic-effect/Google Scholar
9. Talhout, R., T. Schulz, E. Florek, J. van Benthem, P. Wester, A. Opperhuizen. 2011. Hazardous compounds in tobacco smoke. Int. J. Environ. Res. Public Health. 8:613-628.
10. Hautamaki, R.D., D.K. Kobayashi, R.M. Senior, S.D. Shapiro. 1997. Requirement for macrophage elastase for cigarette smoke-induced emphysema in mice. Science 277:2002-2004.
11. Guerassimov, A., Y. Hoshino, Y. Takubo, A. Turcotte, M. Yamamoto, H. Ghezzo, A. Triantafillopoulos, K. Whittaker, J. R. Hoidal, M. G. Cosio. 2004. The development of emphysema in cigarette smoke-exposed mice is strain dependent. Am J Respir Crit Care Med. 170:974-980.
12. Foronjy, R.F., B.A. Mercer, M.W. Maxfield, C.A. Powell, J.D'Armiento, Y. Okada. 2005. Structural emphysema does not correlate with lung compliance: lessons from the mouse smoking model. Exp. Lung Res. 31:547-562.
13. Ma, B., M.J. Kang, C.G. Lee, S. Chapoval, W. Liu, Q. Chen, A.J. Coyle, J.M. Lora, D. Picarella, R. J. Homer, J. A. Elias. 2005. Role of CCR5 in IFN-gamma-induced and cigarette smoke-induced emphysema. J. Clin. Invest. 115:3460-3472.
14. Drannik, A.G., M.A. Pouladi, C.S. Robbins, S. I. Goncharova, S. Kianpour, M. R. Stämpfli. 2004. Impact of cigarette smoke on clearance and inflammation after Pseudomonas aeruginosa infection. Am. J. Respir. Crit. Care Med. 170:1164-1171.