JOURNAL OF PHYSICAL ACTIVITY NUTRITION AND REHABILITATION

Journal of Physical Activity, Nutrition and Rehabilitation, 2017
www.panr.com.cy
info.panr@unic.ac.cy

Coronary Heart Disease Part I: Pathophysiology and Risk Factors

Themistocleous, I.-C[1*]., Stefanakis, M[1]., Douda, H[2].

[1]Department of Life & Health Sciences, University of Nicosia, 46, Makedonitissas Avenue, Nicosia, 1700, Cyprus
[2]Department of Physical Education and Sport Science, Democritus University of Thrace, University Campus, 69100 Komotini, Greece

Abstract

Cardiovascular diseases are the leading cause of disability globally and despite the advances in clinical care and medicine, continue to be the principal cause of morbidity and mortality. The process of this chronic inflammatory condition is initiated early in life by various risk factors. Atherosclerosis is believed to have the main role in the pathogenesis of cardiovascular diseases which involve large and medium sized arteries. Acute coronary events frequently arise and the priority is the re-opening of the occluded artery which will limit the progression of injury. Despite the advances in cardiac surgery, several complications may occur post-surgery. The first part of this article will review the pathophysiology and risk factors of coronary heart disease and the preoperative and postoperative pulmonary complications. The second part will describe the role of physiotherapy in the management of Coronary Heart Disease.

Keywords: Coronary heart disease; anatomy; pathophysiology; acute coronary syndromes; risk factors.

1 Introduction

Cardiovascular Diseases (CVD) are growing radically with an estimation of 12 million people dying each year, mainly in the developing countries (World Health Organisation, 2013). As the burden of CVD growths, coronary heart disease (CHD) is becoming the main cause of cardiac surgery worldwide (Go et al., 2013). Current understanding of the pathophysiological basis of myocardial ischemia is derived from experimental observations that coronary artery narrowing limits coronary blood flow (Gould, Lipscomb & Hamilton, 1974). Understanding these profound mechanisms of disease can help health care professionals identify and treat CVD and prevent potentially complications (Dokken, 2008). This article reviews the pathophysiology and the risk factors of CHD, thus; the pre-operative and post-operative complications of coronary artery bypass graft (CABG).

2 Anatomy of coronary arteries

Coronary arteries are composed by three layers: the tunica intima, tunica media, and tunica adventitia. The tunica intima, which is the innermost layer of the artery, is composed of the endothelium, which acts as the interface between the artery and the blood, and the sub-endothelial layer of connective tissue. The tunica adventitia is mainly composed of collagen fibers, interlaced with bands of elastic fibers. The collagen fibers help to construct a rigid sheath around the artery and restrain the volume of the vessel (Humphrey & McCulloch 2003). The tunica media contains layers of vascular smooth muscle cells

**Corresponding author: e-mail:* irene.them@gmail.com

interspersed in a network of connective tissue and its main role is to produce vasoconstriction or vasodilation of the artery through the contraction or relaxation of the vascular smooth muscle cells (Humphrey & McCulloch 2003).

3 Coronary heart disease

CHD is affecting the coronary arteries, which are supplying oxygenated blood to the cardiac muscle. CHD encompasses atherosclerotic plaques within the coronary arteries, resulting in the stenosis of the artery. Blood flow to the heart is supplied by the right and left coronary arteries, which provide blood on the corresponding side of the heart. Each coronary artery branches into additional arteries, which are responsible to supply with oxygenated blood a specific area of the cardiac tissue. Stenosis and reduced blood supply via any of these arterial segments may have harmful effects on the cardiac muscle and lead to a myocardial infarction (MI) (Libby & Theroux, 2005).

4 Risk factors for coronary heart disease

The risk factors of CHD have been divided into non-modifiable and modifiable (Levy 1981). The non-modifiable risk factors include: age, male sex, and family history which cannot be altered. According to the American Heart Association [AHA] (2009), the modifiable risk factors which can be altered by medical and lifestyle interventions are: hypertension, hypercholesterolemia, physical inactivity, diabetes, overweight, obesity and tobacco smoking. Mora et al. (2007) stated that changes in the modifiable risk factors account for approximately 60% of the risk reduction.

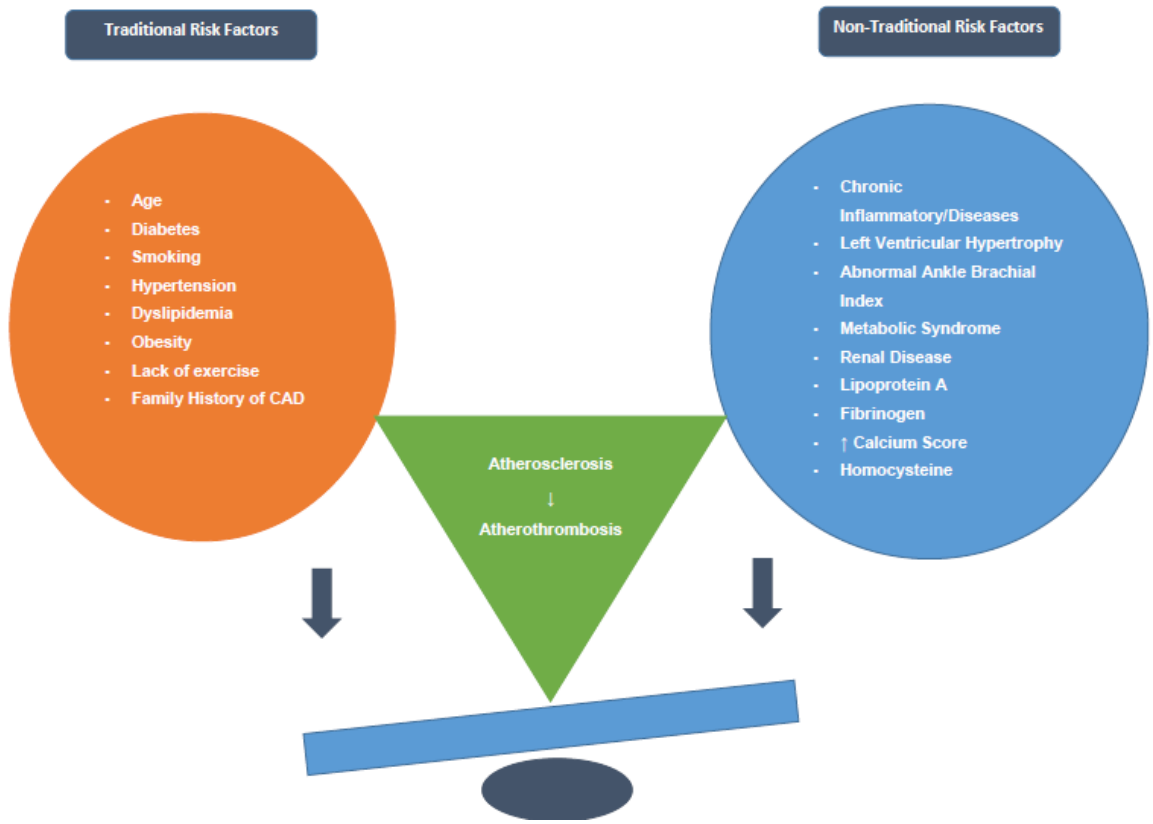

Figure 1. Coronary heart disease risk factors (Adapted from Boudi, 2014).

5 Pathophysiology of coronary heart disease

CHD mainly occurs due to atherosclerosis and its progression is associated with environmental and genetic factors (Sayols-Baixeras, Lluís-Ganella, Lucas, Elosua, 2014). Atherosclerosis is a chronic process, characterized by progressive accumulation of lipids, fibrous elements, and inflammatory molecules in the walls of the large arteries (Glass & Witztum, 2001; Lusis, Mar & Pajukanta, 2004; Sanz, Moreno & Fuster, 2012). Atherosclerosis starts with the efflux of low density lipoprotein (LDL) cholesterol to the sub-endothelial space, which can be changed and oxidized by various agents. Oxidized/modified LDL particles are powerful chemotactic molecules that prompt expression of vascular cell adhesion molecules and intercellular adhesion molecules at the surface of endothelium, and stimulate monocyte adhesion and migration to the sub-endothelial space (Sayols-Baixeras et al., 2014). Monocytes transform into macrophages in the intima media. Macrophages enchain oxidized LDL thru scavenger receptors to become foam cells (Glass & Witztum, 2001) and release pro inflammatory cytokines including interleukins and tumor necrosis factor.

The development of fatty streak which foam cells appear in the sub-endothelial space it is the final result of this process (Sayols-Baixeras et al., 2014). Moreover, in the sub-endothelial space accumulate other forms of leukocytes, including lymphocytes and mast cells (Libby, Ridker & Hansson, 2011). The interaction between monocytes, macrophages, foam cells and T-cells induce a cellular and humoral immune response (inflammatory cascade) with the production of several pro inflammatory molecules such as interleukin-6 (IL-6) and tumor necrosis factor (TNF-α) (Libby, 2012; Witztum & Lichtman, 2013).

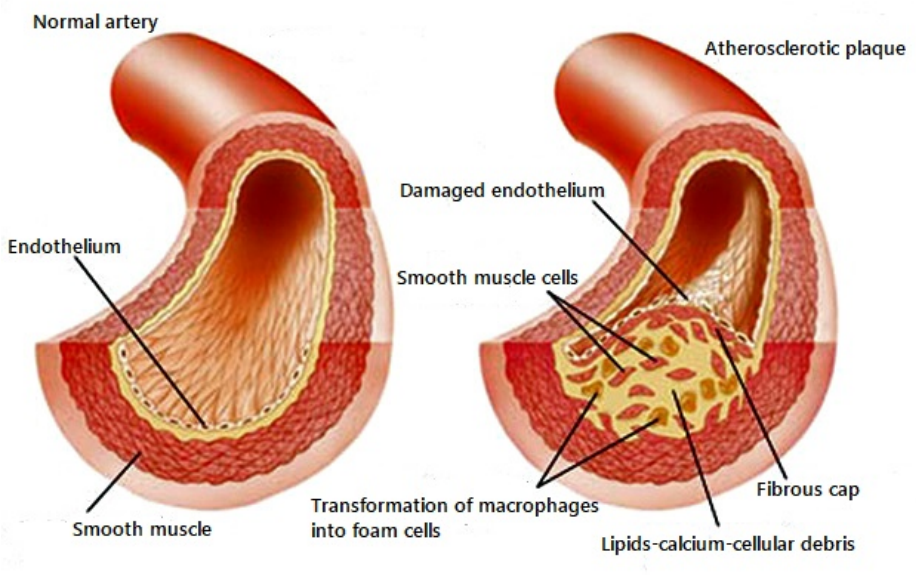

Figure 2. Pathogenesis of atherosclerosis (Modified from Encyclopedia Britannica INC, 2007).

The process continues with the migration of smooth muscle cells from the medial layer of the artery into the intima, following of fatty streak to a more complex lesion (Glass & Witztum, 2001). As soon as smooth muscle cells are in the intima media, they produce

extracellular matrix molecules that are developing a fibrous cap which is covering the initial fatty streak. Inside the fibrous cap the foam cells die, therefore release lipids that collect in the extracellular space, forming a lipid-rich pool (necrotic core) (Tabas, 2010). This process results in the formation of the second atherosclerotic lesion, the fibrous plaque (Sayols-Baixeras et al., 2014). Sakakura et al. (2013) stated that the thickness of the fibrous cap is important for the integration of the atherosclerotic plaque. The extrusion of this type of plaque into the lumen of the artery generates a limitation of flow, well known as stenosis, which is causing ischemia to the tissue and is expressed clinically as stable angina. Moreover, vulnerable plaques composed of a thin fibrous cap made mostly of type I collagen along with no or few smooth muscle cells, but abun¬dant macrophages and pro inflammatory and pro thrombotic molecules leading to atheroma (Sakakura et al., 2013; Witztum & Lichtman, 2013).

Two types of plaque can be defined: stable and unstable or vulnerable, based on the balance between formation and degradation of fibrous cap (Sayols-Baixeras et al., 2014). Stable plaques have an intact, thickset fibrous cap synthesized of smooth muscle cells in a matrix rich in type I and III collagen (Finn, Nakano, Narula, Kolodgie & Virmani, 2010).

Vulnerable plaques are likely to break, revealing the core of the plaque to circulating coagulation proteins, causing thrombosis, sudden artery lumen occlusion and therefore an acute coronary syndrome. Moreover, intraplaque hemorrhage is also a potential factor for the progression of atherosclerosis, (Sakakura et al., 2013; Witztum & Lichtman, 2013), which occur when the vasa vasorum invades the intima from the adventitia (Doyle & Caplice, 2007). Following the diagnosis of acute coronary syndrome the priority is the re-opening of the occluded artery which will limit the progression of injury.Patients can undergo a percutaneous coronary intervention (PCI) or to a coronary artery bypass graft surgery (CABG) (Antman et al., 2004; Hamm et al., 2011).

Despite the advances in cardiac surgery, several complications may occur post-surgery. This review will focus on the postoperative pulmonary complications (PPC).

6 Post-surgery complications

PPC such as atelectasis, bronchospasm and tracheobronchitis can adversely affect patient's condition and may lead to the development of respiratory failure, pulmonary embolism, post-surgery pneumonia, empyema, pneumothorax, acute lung injury, acute respiratory distress syndrome (ARDS), or the need for mechanical ventilation beyond 48 hours' post-surgery (Grooms, 2012). These complications demand carefully individualized strategies to prevent and restore the functional residual capacity (FRC) and patient's ability to mobilize (Grooms, 2012). Procedure related factors are more important than patient related factors in predicting the risk of PPCs (Rudra & Das, 2006). Table 1 summarizes the related risk factors and Table 2 the perioperative pulmonary physiology after thoracic and upper abdominal surgery.

Table 1. Related risk factors

Patient-related factors	Procedure-related factors
• **General health and nutritional status** Age >65 years Low albumin Functional status Weight loss >10% • **Neurological status**	• **Surgical site** Upper abdominal Thoracic surgery • **Surgery technique** Open versus lamparascopic

Impaired sensorium
History of CVA

- **Fluid status**
  CHF history
  Renal failure
  Blood Urea nitrogen
  Blood transfution
- **Immune status**
  Chronic steroid use
  Alcochol use
  Diabetes
- **Chronic lung disease**
  Presence of productive cough
- **Cigarete smoking**
  Current or within 8 weeks
- **ASA class >2**
- **Obesity**
  Body mass index >27.5 Kgm^2
- **Abnormal chest radiograph**
- **Other type of surgery**
  Neck surgery
  Peripheral vascular surgery
  Neurosurgery
- **General anasthesia**
- **Duration of surgery >3hours**
- **Emergerncy surgery**
- **Type of nuromascular blockage**
- **Not using nuroaxial blockade**
- **Pain control with peripheral Narcotics vs epidural anasthesia**
- **Nasogastric tube**

Abbreviations: CVA: Cerebrovascular accident, CHF: Chronic Heart Failure, ASA: American Society of Anesthesiologists classification. Based on Rudra & Das, 2006.

7 Preoperative risk factors

According to Rudra and Das (2006), the pre-operative status of the patient can be a reason for the post-operative complications. Moreover, are stated some other risk factors regarding the operation.

7.1 Respiratory status

Patients with abnormal respiratory findings, such as: wheezing, rales, rhonchi, prolonged expiration, and decreased breath sounds are 6 times more likely to develop a complication, nonetheless the risk differs with the severity of the findings (Eagle et al., 2002).

A significant preoperative risk factor is cigarette smoking, which is often reffered as causative factor of chronic lung disease (Jayr, Matthay, Goldstone, Gold & Wiener-Kronish, 1993; Bluman, Mosca, Newman & Simon, 1998). Reduction of smoking will decrease bronchial irritation and eliminate the stimulus for coughing (Bluman et al., 1998).

Smoking cessation for 48 hours before surgery reduces cough and lowers airway pathogens, decreases the levels of carboxyhemoglobin to normal, eliminates the stimulant effect of nicotine on cardiovascular system, and improves respiratory cilliary beating (Rudra & Das, 2006). According to Warner et al. (1989), patients who stopped smoking for 2 months or less had 4 times higher rate of pulmonary complications, in contrast to those who stopped for more than 2 months (57.1% versus 14.5%).

7.2 Obesity

While Strandberg, Tokics, Brismar, Lundquist and Hedenstiena (1987) found a weak correlation between obesity [calculated by Broca's index: weight (kg)/ (height in cm-100)] and the area of lung densities seen directly after induction of anesthesia; other authors reported that obesity is still a concern for health care professionals. Morbidly obese individuals have a lower FRC, increased alveolar arterial oxygenation gradient and higher intra-abdominal pressure (Rudra & Das, 2006). Eichenberger et al. (2002), stated that in morbidly obese individuals, atelectasis continues for at least 24 hours in contrast to non-obese individuals where atelectasis disappears. Pelosi et al. (1997) reported that the different mechanics of the respiratory system and the hypoxia which can be found in morbidly obese individuals can be explained by the reduced lung volume and by the increased intra-abdominal pressure.

8 Neurological status

Patients with previous stroke and impaired sensorium who are less mobile, have higher risk of atelectasis post-surgery. Moreover, they are unable to protect their airway leading to risk of pneumonia and respiratory failure (Arozullah, Daley, Henderson, Khuri, & National Veterans Administration Surgical Quality Improvement Program, 2000; Arozullah, Conde & Lawrence, 2003).

8.1 Immune status

Alcohol within 2 weeks of surgery increases odds of pneumonia and respiratory failure by 20% (Rudra & Das, 2006). Moreover, alcohol in longer-term may be related with diminished B-cell mediated immunity leading to a greater risk of pneumonia. In addition, patients with diabetes mellitus have a slightly increased risk for respiratory failure (Arozullah et al., 2003).

9 Procedure related risk factors

9.1 Surgery related

The most important factor for the prediction of the overall risk of PPCs is the site of surgery. The rate of complication is related to the distance of the incision from the diaphragm (Rudra & Das, 2006). A decreased post-surgery vital capacity which leads to a ventilation/perfusion (V/Q) mismatch and leads to development of hypoxemia is detected in patients that undergo an upper abdominal and thoracic surgery (Rudra & Das, 2006).

Moreover, several studies show thoracic surgeries have a higher rate of complications in contrast to lower abdominal due to diaphragmatic dysfunction (Dureuil, Viires, Cantineau, Aubier & Desmonts, 1986; Mohr & Jett, 1988; Arozullah et al., 2000). Surgical trauma may enlarge airway reactivity, which can be explained by the exposure to airway irritants (Rock, Freed, Nyhan & Murray, 1995).

9.2 Anesthesia related

The supine posture under anesthesia during surgery modifies the lung volumes, causing impairment of respiratory muscles function, alterations in lung mechanics related to gas exchange, and impairment of mucocilliary clearance mechanisms (Rudra & Das, 2006). The duration of anesthesia also influences the outcome post-surgery. Evidence suggest that longer surgeries lasting more than 3-4 hours are associated with a higher risk of pulmonary complications (Celli, Rodrigue & Snider, 1984; Brooks-Brunn, 1997). Rudra and Das (2006) stated that "after general anesthesia, residual effect of intravenous or

inhalational anesthetics blunt the ventilatory responses to both hypercarbia and hypoxemia. Sedatives augment depression from opioids and anesthetics and might directly depress ventilation". These may lead to airway obstruction, micro aspiration, and ultimately atelectasis, bronchitis and pneumonia (Rudra & Das, 2006).

Table 2. The perioperative pulmonary physiology after thoracic surgery.

• Reduction in vital capacity by 50% to 60% and reduction in functional residual capacity by 30%
• Diaphragmatic dysfunction secondary to reflex inhibition after surgery when viscera are handled close to the diaphragm
• Pain and splinting
• Atelectasis and pneumonia
• Impaired gas exchange and pneumonia
• Impairment of cough and mucocilliary clearance
• Microaspiration

Based on Rudra and Das (2006)

As a conclusion, our understanding of CHD has increased rapidly and current treatments, for this common and troublesome condition is usually offered if coronary events appear. Despite the advances in cardiac surgery, several complications may present post operation. Understanding the multiple effects that general anesthesia and procedure and patients related factors has on the respiratory system is essential, as these problems extend into the postoperative period and can be a reason for complications. These complications may affect patients' quality of life or even cause death.

References

Arozullah, A. M., Conde, M. V., & Lawrence, V. A. (2003). Preoperative evaluation for postoperative pulmonary complications. *Medical Clinics of North America*, *87*(1), 153-173.

Arozullah, A. M., Daley, J., Henderson, W. G., Khuri, S. F., & National VeteransAdministration Surgical Quality Improvement Program. (2000). Multifactorial risk index for predicting postoperative respiratory failure in men after major noncardiac surgery. *Annals of surgery*, *232*(2), 242.

Antman, E. M., Anbe, D. T., Armstrong, P. W., Bates, E. R., Green, L. A., Hand, M., & Jacobs, A. K. (2004). ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction—executive summary: a report of the AmericanCollege of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *Journal of the American College of Cardiology*, 44(3), 671-719.

Bluman, L. G., Mosca, L., Newman, N., & Simon, D. G. (1998). Preoperative smoking habits and postoperative pulmonary complications. *Chest Journal*, 113(4), 883-889.

Boudi FB. (2014b). Coronary artery atherosclerosis. *eMedicine.* Retrieved from http://emedicine.medscape.com

Brooks-Brunn, J. A. (1997). Predictors of postoperative pulmonary complications following abdominal surgery. *CHEST Journal,* 111(3), 564-571.

Celli, B. R., Rodriguez, K. S., & Snider, G. L. (1984). A Controlled Trial of Intermittent Positive Pressure Breathing, Incentive Spirometry, and Deep Breathing Exercises in Preventing Pulmonary Complications after Abdominal Surgery 14. *American Review of Respiratory Disease*, 130(1), 12-15.

Dokken, B. B. (2008). The pathophysiology of cardiovascular disease and diabetes: beyond blood pressure and lipids. *Diabetes Spectrum,* 21(3), 160-165.

Dureuil, B., Viires, N., Cantineau, J. P., Aubier, M., & Desmonts, J. M. (1986). Diaphragmatic contractility after upper abdominal surgery. *Journal of Applied Physiology*, 61(5), 1775-1780.

Doyle, B., & Caplice, N. (2007). Plaque neovascularization and antiangiogenic therapy for atherosclerosis. *Journal of the American College of Cardiology*, 49(21), 2073-2080.

Eagle, K. A., Berger, P. B., Calkins, H., Chaitman, B. R., Ewy, G. A., Fleischmann, K. E., & Leppo, J. A. (2002). *American Heart Association Task Force on Practice Guidelines*. Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery) ACC.

Eichenberger, A. S., Proietti, S., Wicky, S., Frascarolo, P., Suter, M., Spahn, D. R., & Magnusson, L. (2002). Morbid obesity and postoperative pulmonary atelectasis:an underestimated problem. Anesthesia & Analgesia, 95(6), 1788-1792.

Finn, A. V., Nakano, M., Narula, J., Kolodgie, F. D., & Virmani, R. (2010). Concept of vulnerable/unstable plaque. *Arteriosclerosis, thrombosis, and vascularbiology*, 30(7), 1282-1292.

Glass, C. K., & Witztum, J. L. (2001). Atherosclerosis: the road ahead. *Cell,* 104(4), 503-516.

Go, A. S., Mozaffarian, D., Roger, V. L., Benjamin, E. J., Berry, J. D., Borden, W. B., & Turner, M. B. (2013). on behalf of the American Heart Association StatisticsCommittee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2013 update: a report from the American Heart Association. *Circulation*, 127(1), e1-e240.

Gould, K. L., Lipscomb, K., & Hamilton, G. W. (1974). Physiologic basis for assessingcritical coronary stenosis: instantaneous flow response and regional distribution during coronary hyperemia as measures of coronary flow reserve. *The American Journal of Cardiology*, 33(1), 87-94.

Grooms, D. A. (2012). Postoperative Pulmonary Complications. Clinical Foundations: A Patient Focussed Evaluation Program for Respiratory Care Professionals.Available from: http://www.clinicalfoundations.org/assets/foundations13.pdf.

Hamm, C. W., Bassand, J. P., Agewall, S., Bax, J., Boersma, E., Bueno, H., & Hambrecht, R. (2011). ESC Guidelines for the management of acute coronarysyndromes in patients presenting without persistent ST-segment elevation The Task Force for the management of acute coronary syndromes (ACS) in patientspresenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *European Heart Journal,* 32(23), 2999-3054.

Humphrey, J. D., & McCulloch, A. D. (2003). The Cardiovascular System—Anatomy,Physiology and Cell Biology (pp. 1-14). Springer Vienna.

Jayr, C., Matthay, M. A., Goldstone, J., Gold, W. M., & Wiener-Kronish, J. P. (1993). Preoperative and intraoperative factors associated with prolonged mechanical ventilation. A study in patients following major abdominal vascularsurgery. *CHEST Journal,* 103(4), 1231-1236.

Libby, P. (2012). Inflammation in atherosclerosis. *Arteriosclerosis, Thrombosis, and Vascular Biology,* 32(9), 2045-2051.

Libby, P., Ridker, P. M., & Hansson, G. K. (2011). Progress and challenges in translatingthe biology of atherosclerosis. *Nature*, 473(7347), 317-325.

Libby, P., & Theroux, P. (2005). Pathophysiology of coronary arterydisease. *Circulation*, 111(25), 3481-3488.

Lloyd-Jones, D., Adams, R., Carnethon, M., De Simone, G., Ferguson, T. B., Flegal, K., & Hong, Y. (2009). Heart disease and stroke statistics—2009 update a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation,* 119(3), e21-e181.

Lusis, A. J., Mar, R., & Pajukanta, P. (2004). Genetics of atherosclerosis.Annu. Rev. Genomics Hum. *Genet.*, 5, 189-218.

Mohr, D. N., & Jett, J. R. (1988). Preoperative evaluation of pulmonary risk factors. *Journal of general internal medicine*, 3(3), 277-287.

Mora, S., Cook, N., Buring, J. E., Ridker, P. M., & Lee, I. M. (2007). Physical activity and reduced risk of cardiovascular events potential mediating mechanisms. *Circulation,* 116(19), 2110-2118.

Moreno, A. M., Castro, R. R., Sorares, P. P., Sant'Anna, M., Cravo, S. L., & Nóbrega, A. C. (2011). Longitudinal evaluation the pulmonary function of the pre- and postoperative periods in the coronary artery bypass graft surgery of patients treated with a physiotherapy protocol. *J Cardiothorac Surg*, 6, 62.

Rock, P., Freed, A. N., Nyhan, D. P., & Murray, P. A. (1995). Thoracotomy increases peripheral airway tone and reactivity. *American journal of respiratory and critical care medicine,* 151, 1047-1047.

Rudra, A., & Sudipta, D. (2006). Postoperative pulmonary complications. *Indian J Anaesth,* 50(2), 89-98.

Sanz, J., Moreno, P. R., & Fuster, V. (2012). The year in atherothrombosis.Journal of the *American College of Cardiology*, 60(10), 932-942.

Sakakura, K., Nakano, M., Otsuka, F., Ladich, E., Kolodgie, F. D., & Virmani, R. (2013). Pathophysiology of atherosclerosis plaque progression. *Heart, Lung and Circulation*, 22(6), 399-411.

Sayols-Baixeras, S., Lluís-Ganella, C., Lucas, G., & Elosua, R. (2014). Pathogenesis of coronary artery disease: focus on genetic risk factors and identification of genetic variants. *The application of clinical genetics*, 7, 15.

Strandberg, Å., Tokics, L., Brismar, B., Lundquist, H., & Hedenstierna, G. (1987). Constitutional factors promoting development of atelectasis during anaesthesia. *Acta anaesthesiologica scandinavica*, 31(1), 21-24.

Tabas, I. (2010). Macrophage death and defective inflammation resolution in atherosclerosis. *Nature Reviews Immunology*, 10(1), 36-46.

Warner, M. A., Offord, K. P., Warner, M. E., Lennon, R. L., Conover, M. A., & Jansson Schumacher, U. (1989). Role of preoperative cessation of smoking and other factors in postoperative pulmonary complications: a blinded prospective study ofcoronary artery bypass patients. In Mayo Clinic Proceedings (Vol. 64, No. 6, pp. 609-616). Elsevier.

Witztum, J. L., & Lichtman, A. H. (2013). The influence of innate and adaptive immune responses on atherosclerosis. *Annual review of pathology,* 9, 73-102.

World Health Organization. (2013). Cardiovascular disease. Retrieved March 20th, 2013 from http://www.who.int/ncd/cvd/.