CHAPTER I BACKGROUND

1.1. Background

Acute ischemic limb disease is one of cardiovascular diseases that need reperfusion as the first action to help (Zhang *et al.*, 2013). Fogarty balloon catheter is widely known to make reperfusion in blood vessel and it give real impact in vascular surgery aimed at removing material, which inhibits blood flow with only a small incision (Bunt, 1990; Rutherford, 2010).

Clinical experience demonstrates the use of a balloon catheter embolectomy safe and effective (Bunt, 1990), but on the other hand can lead to various complications such as endothelial denudation, intimal damage, thrombosis (Shea, 2012), and intimal thickening (Bunt, 1990; Doornekam *et al.*, 1996; Chlupac *et al.*, 2009; Chen *et al.*, 2013).

Intimal thickening is the process by which the cell population increases (hyperplasia) within the innermost layer of the arterial wall (Newby and Zaltsman, 2000). The trauma caused by several times development and withdrawal of the repeated Fogarty balloon catheter in tunica intima, media, and adventitia (White and Hollier, 1994; Burnstock, 2002). As a result of this treatment there is damage to the endothelial layer that triggers the migration and proliferation of vascular smooth muscle cells (VSMC) and increase in deoxyribonucleic acid (DNA) synthesis that is regulated by growth factors (Newby and Zaltsman, 2000; Haga *et al.*, 2003). The migration of VSMC into tunica intima could develop into intimal hyperplasia that leads to atherogenesis (Bunt 1990; Burnstock, 2002).

L-arginine which known as the substrate of a family of enzymes named nitric oxide synthases (NOS) (Boger, 2007; Debats *et al.*, 2009; Huang *et al.*, 2009). The formation of NO in endothelial need L - Arginine which catalyzed by endothelial NOS (eNOS) (Napoli *et al.*, 2013). Nitric oxide has a wide range of biological properties that maintain vascular homeostasis, protection of the vessel from injurious consequences of platelets and cells circulating in blood (Jerca *et al.*, 2002), maintain normal endothelial function (Jerca *et al.*, 2002), inhibit contraction of blood vessel and platelets adhesion to the endothelium surface (Alderton *et al.*, 2001), and inhibits proliferation and migration of VSMC (Huang *et al.*, 2009; Lei *et al.*, 2013; Napoli *et al.*, 2013). Nitric oxide can reduce hyperplasia by utilizing its role as apoptotic and necrotic cell death (Wang *et al.*, 2010; Napoli *et al.*, 2013).

This research conducted to use rabbits as the experimental model in purpose to improve the ability and quality of human life through animal model. As the ethics code of Veterinary in Indonesia "Manusya Mriga Satwa Sewaka" (PDHI, 2010), which means giving devotion as a veterinary for community, state, and nation through the animal world as the fundamental base of the research. In the future, this treatment that applied to humans is very likely to be applied to cure the animals along with the strengthening of animal welfare and increasement of pet lover.

Based on the background above the research entitled “Effect of Oral Administration of L-arginine on The Blood Vessels’ Wall Thickness Post Fogarty balloon catheter in Rabbit (*Oryctolagus cuniculus*) Iliac Arteries” conducted.

1.2. Problem Statement

Does L-arginine have effect decreases the vascular's wall thickness of rabbit iliac artery post Fogarty balloon catheter?

1.3. Theoretical Base

The damage in the endothelial monolayer caused by experimental balloon embolectomy catheter result chronic dysfunction of the endothelial L-arginine/NO pathway that plays a causative role in the development of intimal hyperplasia. The regeneration of endothelial cell lead to diminish production and release of NO that in long-standing deficiency contributes to the excessive growth of VSMC. Dysfunction of the L-arginine/NO axis at the site of injury may result in loss of a critical inhibitor of VSMC proliferation (Tarry *et al.*, 1994).

L-arginine is indispensable as the endogenous NO and inducible NOS (Alderton *et al.*, 2001; Jerca *et al.*, 2002; Napoli *et al.*, 2013). Nitric oxide (NO) regulates many functions, such as vascular tone, blood pressure, neurotransmission, immune response, oxidation-sensitive mechanisms, protecting cells (Jerca *et al.*, 2002), and inhibits proliferation and migration of VSMC (Boger, 2007 and Napoli *et al.*, 2013).

The function of inhibit proliferation and migration of VSMC is because the NO could perform apoptotic and necrotic toward cells (Wang *et al.*, 2010; Napoli *et al.*, 2013). Since the injury of blood vessel walls it giving important signal then occurs the luminal stenosis and occlusion (Bunt, 1990; Doornekam *et al.*, 1996). Intimal hyperplasia may be defined as the abnormal migration and proliferation of VSMC with associated deposition of extracellular connective

tissue matrix (Napoli *et al.*, 2013). Vascular smooth muscle cells migrate to populate the intima, either from the media or from the circulation (Haga *et al.*, 2003; Gerthoffer, 2007; Louis and Zahradka, 2010). Therefor the exceeded amount of proliferating VSMC would trigger NO activation then transfected into cell's mitochondria that lead to cell apoptosis (Napoli *et al.*, 2013). This action indicates that NO is an essential negative regulator of cell precursor proliferation during or post trauma (Peunova, 2001).

1.4. Research Objective

The objective of this research is to prove the effect of L-arginine decreases the blood vessels' thickness post Fogarty balloon catheter in rabbit iliac arteries through histopathological observation using Hematoxylin and Eosin (HE) staining.

1.5. Benefit of Research

1. Provide information effectiveness of oral administration of L-arginine in suppressing the thickening of blood vessel's wall.
2. As an alternative adjunctive therapy in preventing forming of arteriosclerosis of patients after performing Fogarty balloon catheter.
3. As comparative medic for human health development.

1.6. Hypothesis

The hypothesis proposed that L-arginine decreases the thickness of blood vessel's wall post Fogarty balloon catheter in rabbit iliac arteries.