Annals of Surgery and Perioperative Care

Open Access

Austin Publishing Group

Review Article

Study on Pressure Overload-Induced Cardiac Hypertrophy Model by Applying Transverse Aortic Constriction and O-ring Ascending Aortic Banding Technique: A Comparative Analysis

Anas Rashid*
School of Medicine (Vascular Surgery), University of Turin, Turin, Italy

***Corresponding author:** Anas Rashid (Vascular Surgery), Graduate School of Medical Science and Engineering, College of Life Science and Bioengineering, Korea Advanced Institute of Science and Technology, Daejeon, Republic of Korea

Received: June 27, 2020; **Accepted:** October 17, 2020; **Published:** October 24, 2020

Abstract

Left-ventricular cardiac hypertrophy is a well-established precursor of heart failure with the ominous prognosis. To develop the surgical procedure that can easily and efficiently replicate this condition is too critical, and is significantly important for the better understanding of the pathophysiological mechanisms associated with this vascular disease. Constriction of the aorta in mice is a highly accepted method for the creation of pressure overload-induced cardiac hypertrophy model. The two microsurgical procedures available for the successful development of the disease model are aortic constriction at the level of transverse aorta and o-ring aortic banding using the ascending aorta. The transverse aortic constriction has many advantages over the other available technique which is significantly highlighted in this paper. Using transverse aorta, though the degree of constriction is widely dependent on the diameter of the gauge needle. Our main purpose is to establish a comparison between these two surgical procedures to highlight the highly reproducible and precise method to study the mechanism of the disease progression as well as cardiac remodeling.

Introduction

Vascular diseases are the major cause of mortality and morbidity and associated with high societal costs [1]. The understanding of the pathological mechanism's underlying cardiovascular remodeling; although critical but essential for the development of innovative therapies for vascular diseases [2]. At the first phase of this pathological cardiac remodeling process, the heart undergoes hypertrophic growth through each myocytes enlargement which does not affect the normal function of the heart. The main purpose of this remodeling is to enhance the cardiac pump function [3]. However, the continued stress would lead to the fibrosis and enlargement of the heart chamber.

Reproducibility is expected in research related to heart diseases, and validity, and accuracy, is of great concern [2]. It is well established that related conduits control the vasculature and heart development in mice and humans. Therefore, preclinical studies continue to rely heavily on mouse models and thus these models are useful both for the development of drugs with the study of mechanism [4]. Since the heart has a negligible capacity of regeneration, most form of cardiac injury ultimately results in fibrosis development [2-4]. The further development of novel and innovative techniques would also highlight major steps forward in the modeling of vascular diseases.

In cardiovascular research, surgically induced models of heart failure are widely used. Constriction of the aorta is a well-recognized method for left ventricular hypertrophy induction in mice [5]. As in the left ventricular chamber, increased blood pressure ultimately leads to the development of this condition, and it also mimics the similar condition in humans which results in the chronic systemic hypertension or aortic stenosis [4].

There are three different positions for the creation of aortic constriction, these are descending aorta, ascending aorta and transverse aorta [6]. Among this, one of the most common surgical models of heart failure and pressure overload-induced cardiac hypertrophy, is the constriction at the level of the transverse aorta which is widely known as Transverse Aortic Constriction (TAC). Thus, for the successful creation of pressure overload in the left ventricle, constriction on a permanent basis around the transverse part of the aorta must be achieved which further limits the blood outflow towards the left ventricle [3-5]. TAC can produce cardiac diastolic and systolic dysfunction and long-term progression to heart failure in addition to cardiac remodeling effects such as fibrosis and hypertrophy [4].

The other method used for the development of the disease in mice is the ascending aortic constriction through o-rings with fixed inner diameters which is known as O-Ring Aortic Banding (ORAB). Hence, our aim is to compare two most important aortic constriction methods to highlight the highly reproducible and precise method to study the mechanism of the disease progression as well as cardiac remodeling.

Methodology

Latest reports indicate a substantial association between ethnic backgrounds or race and the hypertrophy development, which

Citation: Rashid A. Study on Pressure Overload-Induced Cardiac Hypertrophy Model by Applying Transverse Aortic Constriction and O-ring Ascending Aortic Banding Technique: A Comparative Analysis. Ann Surg Perioper Care. 2020; 5(1): 1043.

strongly suggests the presence of genetic modification upon the pressure overload-induced left ventricular hypertrophy and cardiac remodeling [1-3]. Many researchers use genetically engineered mice models maintained on mixed-bred and out-bred backgrounds, therefore, variability on the genetic basis may also contribute towards cardiac response after the constriction of the aorta [2-4].

In order to generate genetically engineered mice, 129S1/svImJ and C57BL/6J inbred strains are most widely used for this purpose, but various studies are also done on mixed background mice such as 129S1 and B6 [6]. Overall, mice of any background can be used for the surgical procedure of aortic constriction. Hence, the surgical procedure can be accomplished on knock-out, wild-type, and transgenic mice but additional preventive measures should be taken in immunosuppressive transgenic mice [3-5].

12-16 weeks old, male adult mice are ideal for this surgical procedure due to the complete development of heart and the mice' weight may range between 24 to 26 g. Female adult mice can also be used, but they are not ideal as many studies suggested that they are less likely to develop cardiovascular diseases [6]. Since the procedure of aortic surgery is relatively short as compared to other surgical procedures, it is not required to withhold from mice both water and food prior to the procedure [3].

Here, we have compared the methods of aortic constriction in mice. The two well established methods are transverse aortic constriction and ascending aortic constriction. Besides these two methods, researchers can also choose between slipknot technique as well as abdominal aortic banding.

A study conducted by Richards and colleagues elegantly explained the transverse aortic constriction method. They mentioned that mice were ventilated and intubated at 2% isoflurane and 98% of oxygen saturation level respectively [4]. They first made small midline skin incision just above the thorax and both muscles i.e. intercostal as well as pectoral muscles were gently separated and dissected bluntly [3]. Using fine retractor, ribs were retracted and gradually the transverse aorta was identified by its posterior location to thymus gland [2]. After successful identification of transverse aorta, the next step was the placement of 7-0 nylon suture between the left common carotid artery and brachiocephalic trunk [4]. Around the transverse aorta, two loose knots were tied, and then blunt-ended 25G, 26G or 27G needle which was pre-sterilized was placed parallel to the transverse aorta [3]. After cautiously achieved the double knot against the needle, quickly detached the needle in order to produce aortic constriction. As they mentioned, this method slightly increase the flow of blood towards the right common carotid artery and eventually to the head, neck and face [6]. The chest retractor was removed and the ribcage, skin and associated muscles were closed by using 6-0 absorbable nylon suture.

The other study conducted by Melleby and colleagues showed that uniform aortic banding can be achieved by using o-ring around the ascending aorta. They first prepared the o-rings by simply cut the ring at the lateral position and nylon 6-0 suture was placed to the opening cut at a parallel angle. They used the same approach as done by previous researchers except the ascending part of the aorta was accessed through 3rd intercostal space. After careful identification of the ascending aorta, the o-ring was placed and the upper and lower suture was tied gradually so that o-ring can be closed easily. The other procedure was same for the closure of muscles, ribcage as well as skin [2].

Both methods showed the effective development of disease in mice. Perhaps, aortic constriction at the level of transverse aorta remains the standard pressure overlord-induced cardiac hypertrophy model and it is widely accepted. While, O-ring banding method is technically demanding, difficult to reproduce and it also lead to aortic complications such as trauma.

Discussion

In this paper, we included two methods for the development of pressure overload-induced cardiac hypertrophy model in mice. Since, Rockman and colleagues published first research on aortic constriction and they mentioned surgical procedure via transverse part of the aorta [3]. Afterwards, this surgical technique is widely accepted due to less invasive, but with the o-ring banding method, the echocardiographic as well as hemodynamic measurement cannot performed with high reproducibility [2]. Still further investigation is required for pharmacological and genetic intervention.

One of the preferred method to study the mechanisms of heart disease is the aortic constriction [3]. Although, this surgical procedure can be performed in rats, rabbits and guinea pigs, but in mice it can be modified genetically. The main focus is to reduce the trauma associated with TAC. As this is greatly dependent on the tightness of the suture against the needle [4]. In comparison to ORAB, the constriction is highly dependent on the internal diameter of the o-ring. Some studies shows that this would lead to the consistent disease progression and cardiac remodeling, but it raises several question especially related to the degree of trauma to the aorta.

Using TAC procedure, researchers not only observed hypertrophy however, also marked cardiac fibrosis with the increased mass of the lungs which is related to pulmonary edema condition. This greatly suggests that the transverse aortic constriction surgical procedure is particularly valuable in both preclinical drug development as well as pathological mechanisms of cardiac failure [5].

Different strains of mouse respond quite differently towards the cardiac hypertrophy model and therefore, both the difference in sex and strain are major concern with these procedures. Generally compared to other available methods of cardiac failure, such as a chemical-induced hypertrophy model and ligation of the left anterior descending coronary artery, TAC provides moderate pressure overload on left ventricle and also allows gradual development of heart failure without any off target effects. Even though, this procedure is surgically challenging but with usual practice, one can attained survival rate up to 80 to 90% [1].

Additionally, o-ring banding of aorta produces excessive stretching of left ventricle and myocardial damage that greatly affect the reproducibility of the results [2]. It also reduces the survival of the mice mainly due to rupture to the aorta. This technique is demanding as well, as it requires well trained personnel and surgical variables are also critical therefore, only a minor surgical error will lead to the death of the animal.

To summarize, both techniques have some advantages and disadvantages to one and other. Many studies reports that TAC is more efficient and it generates consistent and homogenous stenosis of aortic arch. Therefore, this technique provides stable and fully controlled aortic constriction. So, this microsurgical procedure can be easily completed with basic surgical understanding.

References

1. Richards DA. Distinct phenotypes induced by three degrees of transverse aortic constriction in mice. Sci Rep. 2019; 9: 5844.
2. Melleby AO. A novel method for high precision aortic constriction that allow for generation of specific cardiac phenotypes in mice. Cardiovasc Res. 2018; 114: 1680-1690.
3. Merino D. Experimental modelling of cardiac pressure overload hypertrophy: Modified technique for precise, reproducible, safe and easy aortic arch banding-debanding in mice. Sci Rep. 2018; 8: 3167.
4. Schnelle M. Echocardiographic evaluation of diastolic function in mouse models of heart disease. J Mol Cell Cardiol. 2018; 114: 20-28.
5. Koentges C. Gene expression analysis to identify mechanisms underlying heart failure susceptibility in mice and humans. Basic Res Cardiol. 2018; 113: 8.
6. Ardehali H. Manual of Research Techniques in Cardiovascular Medicine. John Wiley & Sons, Ltd. 2014.
7. Patten RD, Hall-Porter MR. Small animal models of heart failure: development of novel therapies, past and present. Circ Heart Fail. 2009; 2: 138–144.
8. Calamaras TD. Mixed Lineage Kinase 3 (MLK3) Prevents Cardiac Dysfunction and Structural Remodeling with Pressure Overload. Am J Physiol Heart Circ Physiol. 2018.
9. Furihata T. Te experimental model of transition from compensated cardiac hypertrophy to failure created by transverse aortic constriction in mice. Int J Cardiol Heart Vasc. 2016; 11: 24–28.
10. Eichhorn, L. A Closed-chest Model to Induce Transverse Aortic Constriction in Mice. J Vis Exp. 2018.
11. Zhang M. Both cardiomyocyte and endothelial cell Nox4 mediate protection against hemodynamic overload-induced remodelling. Cardiovasc Res. 2018; 114: 401–408.
12. Byrne NJ. Normalization of cardiac substrate utilization and lef ventricular hypertrophy precede functional recovery in heart failure regression. Cardiovasc Res. 2016; 110: 249–257.