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RESEARCH ARTICLE

DEVELOPMENT OF A NOVEL MITRAL VALVE REPAIRMENT DEVICE WITH DELIVERY SYSTEM FOR THE TREATMENT OF MITRAL VALVE REGURGITATION: AN IN-VITRO SAFETY ASSESSMENT

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ABSTRACT

Mitral valve prolapsed is a prevalent condition that leads to mitral regurgitation, resulting in the backflow of blood into the left atrium. This condition imposes an increased workload on the heart, potentially leading to the weakening of the heart muscle over time. In this research study, we have presented a concise depiction of a novel mitral valve repairing device designed specifically for the treatment of mitral valve regurgitation. The proposed implant incorporates various components, including a fastener, a slotted nut, multiple crowns and anchors which are interconnected in a predefined manner to enable circular expansion of the implant. The V-shaped structure of the crowns ensure the equal stress distribution during leaflet actuation & minimizing the risk of tissue wall damage. The circularly expandable nature of the implant allows for effective treatment of annular regurgitation of the mitral valve within the native annulus. In order to evaluate the safety and efficacy of the MVR device, in-vitro testing was conducted. This approach allowed the study to be ethically viable while ensuring relevance to human physiology, cost-effectiveness, a controlled experimental environment, risk identification and mitigation, and adherence to regulatory requirements. The preliminary findings obtained from this in vitro testing provided valuable insights into the safety profile of the mitral valve repairment device.

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INTRODUCTION

The human heart comprises four essential valves, namely the tricuspid, bicuspid (mitral), aortic, and pulmonary valves, each playing a crucial role in maintaining proper blood flow. Mitral regurgitation, characterized by the incomplete closure of the mitral valve leaflets, results in abnormal backward blood flow from the left ventricle to the left atrium. This condition poses a significant health risk as the left ventricle fails to adequately pump blood while excess blood flows back into the left atrium. Mitral valve regurgitation is the most common valvular abnormality worldwide, affecting over 2% of the total population and has a prevalence that increases with age. It can be caused by various factors, including valve prolapse, damaged tissue cords, rheumatic fever, endocarditis, abnormalities of the heart muscle and heart failure. The severity of the condition determines the appropriate treatment approach. Mild leakage is typically managed with medications aimed at improving heart function. However, in cases of acute leakage, surgical intervention may be necessary. Traditionally, open heart surgeries have been the standard approach for cardiac operations, involving invasive procedures such as median sternotomy or thoracotomy. These procedures are associated with postoperative pain, medical complications and prolonged recovery periods. Additionally, patients in poor medical condition may not be eligible for open heart surgery due to the associated risks, depriving them of much-needed surgical treatment for their heart disease. Currently open heart mitral annuloplasty is being done which involves more risk and increase bedtime for the patient. To address these challenges, transcatheter-based approaches have emerged as a minimally invasive alternative for mitral valve regurgitation surgery. The present research focuses on one such approach that involves repairing and reshaping the native annulus of mitral valve using a transcatheter technique. This approach aims to enhance the closure of mitral valve leaflets by replacing supportive cords or removing excessive valve tissue, thereby reducing valve regurgitation. Moreover, annular reduction, achieved by attaching an artificial annuloplasty ring to the mitral valve annulus or utilizing a clip to close the leaflets, enables effective reshaping of the mitral valve. The present invention offers a minimally invasive approach rather than open heart surgery, it will lessen the overall procedure time and hospital stay of the patient will also decrease. The risk will also be less compared to open heart surgery. One can adjust the device if there is any further prolapse where in other device one cannot adjust the device and has to be replaced by doing open heart surgery. By utilizing transcatheter techniques for mitral valve regurgitation surgery, the operation time can be significantly reduced compared to conventional open heart procedures. This approach offers a promising alternative for patients who are not suitable candidates for open heart surgery or desire a less

invasive treatment option. The purpose of this study is to evaluate the efficacy and safety of the transcatheter approach in treating mitral valve regurgitation, highlighting its potential to revolutionize the management of this critical cardiac condition.

MATERIALS AND METHOD

In the context of treating mitral valve regurgitation, a semi-rigid frame is utilized as an implant to address the condition. Its primary purpose is to reshape and reconnect the valve leaflets, thereby mitigating the backward flow of blood from the left ventricle to the left atrium. This is achieved by reducing the diameter of the mitral valve annulus, which serves as a pivotal factor in determining the appropriate size of the implant. It is crucial to note that the diameter of the semi-rigid frame implant plays a critical role in the success of the procedure. If the implant diameter exceeds the optimal size, it can impose excessive strain on the heart, potentially leading to sudden heart failure. Conversely, if the implant diameter is too small, the patient may not experience any noticeable improvement following the implantation of the semi-rigid frame. To execute the treatment, the semi-rigid frame is positioned on the surface of the mitral valve annulus, strategically placed between the left atrium and left ventricle. This placement is essential as it enables the reduction of regurgitation by promoting leaflet coaptation and readjusting the overall shape of the mitral valve. By doing so, the semi-rigid frame aims to restore normal valve function and enhance blood flow efficiency. The circular expandable Mitral valve repair device depicted in Figure.1 comprises several distinct components that work together to achieve its intended purpose. These components include a bolt assembly, sleeves, crowns and a coil screw. This assembly is constructed of different materials such as both Stainless Steel (SS) and Nitinol alloy. The selection of material depends on various factors, including durability, biocompatibility and mechanical properties.

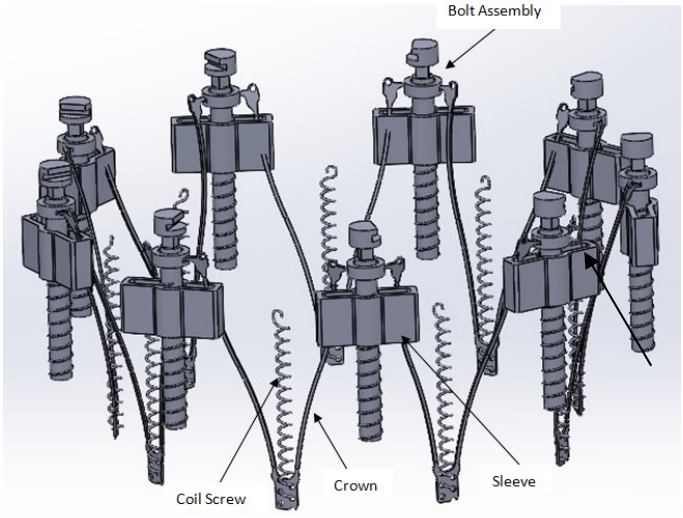

Figure 1. Distinct components within the Mitral Valve Repair Device

Bolt assembly: The bolt assembly is made up of a metallic material but not limited to stainless steel (SS), nitinol or cobalt chromium (CoCr) alloy or combinations thereof. It is comprised of a free ring that serves a crucial role in activating the implant after the anchoring process is completed. This free ring allows for controlled expansion and adjustment of the device within the mitral valve structure. By manipulating the free ring, the device would be appropriately positioned and deployed to achieve the desired outcome.

Sleeves: The sleeve is made up of a metallic material but not limited to 316L SS, 316LVM SS, 304 SS, Nitinol. It consists of internal threads that interlock with the external threads of the bolt which have same the pitch which will be in a range of 0.3mm to 0.8mm. These threaded components form a secure connection, allowing them to be tightly joined together. In addition to the threaded design, the sleeve incorporates two side slots on its inner surface. These slots serve a specific purpose: they provide a clear pathway for the crown arms that are intended to be welded to the bolt assembly. By having these side slots, the sleeve enables the crown arms to be properly positioned and aligned with the bolt, facilitating the welding process and ensuring a precise and accurate assembly. The sleeve may include a predefined height ranging from 3 mm to 6mm.

Crowns: The crowns, which are components of the assembly, are specifically welded at the free ring. The crowns can be made up of a biocompatible metallic material but not limited to SS (stainless steel) alloy, nitinol alloy (TiNi-SS, TN3, TNC, TiNi-YY, Ti-Ni-01, 5 and Ti-Ni-02), CoCr (cobalt chromium) alloy, etc. It may include a proximal end, a distal end and a predefined length may be in a range of 18 mm to 25 mm. This free ring is designed with a lower thickness compared to other parts of the assembly. The intention behind this lower thickness is to minimize the stress exerted on the native annulus, the natural tissue surrounding the implant. By reducing the stress, the chances of damaging the native annulus tissue are significantly decreased, promoting the overall longevity and health of the surrounding tissue. Furthermore, the lower thickness ranging from 300 microns to 750 microns of the free ring also contributes to an increased tissue growth rate over the device. This means that the native tissue is more likely to grow and integrate with the implant more effectively, leading to better long-term outcomes. To enhance radiopacity, the laser-cut crowns feature a circular cavity on their proximal end. This cavity serves as a convenient location to attach markers. These markers are specifically utilized to enhance the visibility of the device under imaging techniques such as fluoroscopy. By incorporating markers in the circular cavity, the implant becomes more visible, aiding in accurate positioning and monitoring during medical procedures.

Coil screw: The coil screw can be made up of metallic material, including, but not limited to, 316L SS, 304 SS, 316LVM SS, etc. The length of the coil screw will be in a range of 5mm to 20mm. It is manufactured by coiling a wire of diameter ranging between 0.1mm to 0.4mm. The anchoring process of the assembly is facilitated by a coil screw, which plays a crucial role in ensuring a secure and stable attachment. The coil screw features a specific pitch, referring to the distance between the turns of the spring. This pitch is carefully chosen to enable smooth and controlled anchoring as the coil screw is inserted through the designated holes in the frames. The pitch allows for precise alignment and movement of the screw, ensuring effective placement and reducing the risk of complications. At the distal end of the spring, there is a sharp edge located at the bottom. This design feature serves a specific purpose: it assists in the penetration of the mitral valve annulus tissue. The sharp edge of the spring allows for easier entry into the annulus, facilitating the anchoring process and providing a secure attachment point. This sharp edge is designed to minimize tissue trauma while effectively engaging with the annular tissue. On the other hand, at the proximal end of the spring, a hook-type design is implemented. This hook serves as a mechanism to rotate the spring during the procedure, employing the aid of a delivery system. The hook allows for controlled manipulation and positioning of the spring within the target area, ensuring accurate placement and optimal alignment. This design feature enhances the precision and reliability of the anchoring process, promoting successful outcomes in the treatment of mitral valve-related conditions.

Assembly of the components: In the initial stages of the assembly process, the springs are carefully incorporated into the crowns, ensuring that holes are positioned at the distal end of the frames. Each spring consists of two distinct ends, namely the proximal loop end and the distal sharp end. The proximal loop end serves the purpose of maneuvering and propelling the spring forward, allowing it to attain its intended anchored position within the native annulus of the mitral valve. On the other hand, the distal sharp end is designed to facilitate the insertion of the spring into the native annulus, effectively securing it in place. This sharp end possesses the necessary strength and pointedness to aid in insertion and ensure the device remains firmly

fixed. Moving on to the bolt sub-assembly, it comprises a bolt, a free ring and a bolt head. Initially, the bolt is equipped with a resting pad to accommodate the Free State ring and these two components are assembled together. Following this, the bolt head is inserted into the bolt cavity, permanently welding it to the bolt. Once these steps are completed, the bolt assembly is prepared for integration with the crowns. In addition, the sleeve component possesses a cavity that features slots and threads. Each individual crown is joined to the sleeve by placing its respective arm into the slots. Subsequently, the bolt assembly is introduced into the sleeve, forming a secure connection. The crown head is then welded to the free ring of the bolt, finalizing the assembly process. This sequence of assembly and sub-assembly is repeated for the crowns, resulting in the formation of a circular, semi-rigid frame. The inclusion of crowns in the device is crucial as it provides sufficient strength. This ensures that the spring anchors firmly grip the annulus even under the pressure exerted by the blood flow. By distributing the load across multiple crowns, the chances of device migration are significantly reduced. Insufficient crowns, on the other hand, would place greater stress on the implant, potentially compromising the proper closure of the damaged valve and impeding the patient's relief. Furthermore, a lower number of crowns may increase the risk of the anchor component damaging the native annulus of the mitral valve, thereby elevating the possibility of migration. We assert that a mitral valve repair device should comprise a total of six to nine crowns to effectively manage the stress exerted on the implant.

The Delivery system: Figure.2 depicts a delivery system composed of several interconnected components. These components include threaded rollers, a guided plate and a handle casing. The threaded rollers are positioned at two specific locations within the casing, namely proximal and distal. Each roller consists of two distinct ends: a plain shaft and a threaded shaft. The threaded shaft enables rotational movement in both clockwise and counter-clockwise directions & plain shaft of the roller enables axial movement on forward and backward directions. The rollers of the delivery system are attached to various implant components, including a coil screw, a bolt assembly and a singular bolt assembly. The plain shaft of the roller allows for axial movement in the forward and backward directions.

The proximal rollers are connected to the coil screw through the use of wires. Their purpose is to anchor the coil screw of the implant to the annulus of the mitral valve. On the other hand, the distal rollers are connected to the bolt head using wires. They are responsible for actuating the bolts by imparting circular motion to the bolt, thereby causing the sleeve to move downward and actuate the frame. The guided plate is positioned between the rollers and the implant. Its primary function is to guide the wires to their respective components and facilitate independent movement of the implant. The device has a Femoral Access with 27 Fr Catheter.

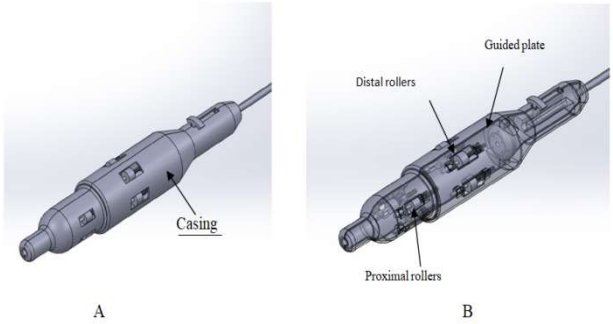

Figure 2. Streamlined Delivery for Mitral Valve Repair: A Comprehensive Approach

RESULTS AND DISCUSSION

The study involved the use of an intricate in-vitro tissue model replicating the structure of the mitral valve. This model consisted of leaflets that initially had a diameter of 38 mm.

To simulate a realistic scenario, a specially designed implant was created. This implant was circular in shape and could expand when needed, with a diameter of 40 mm. The implant was carefully introduced into the in-vitro tissue model using an aforementioned delivery system specifically designed for this purpose. It was crucial to position the implant accurately above the mitral valve leaflets to ensure proper functionality. Anchors were utilized to secure the implant in place. These anchors were precisely placed and firmly fixed onto the leaflets of the in-vitro model to provide stability. Once the anchoring process was completed, the next step involved activating the implant. This activation was achieved by rotating the fasteners attached to the implant. To facilitate this rotation, a spanner tool was employed. As the fasteners were rotated, the sleeves attached to them moved in a downward direction. The downward motion of the sleeves caused the expanded crowns of the implant to actuate. This actuation resulted in a reduction of the leaflet diameter from the initial 38 mm to a new diameter of 30 mm. In summary, the study successfully demonstrated the ability to manipulate and adjust the size of the mitral valve leaflets using the implant and its associated mechanisms. Figure.3 illustrates in-vitro implantation of Mitral Valve Repair Device into the mitral valve.

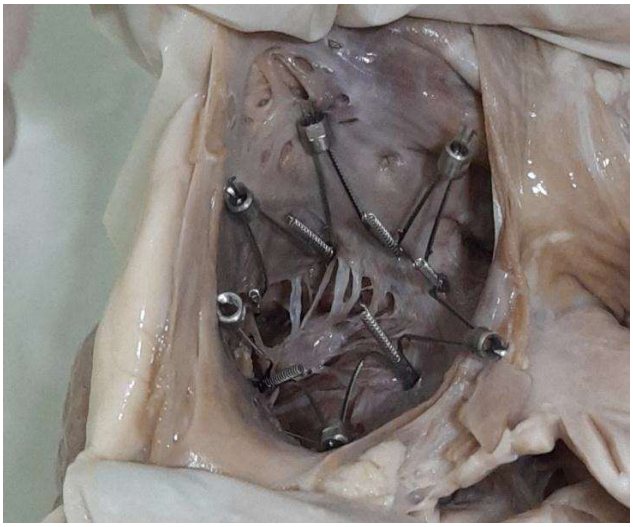

Figure 3. Implanting Expanded Mitral Valve Repair Device within the Mitral Valve into an in-vitro tissue model

CONCLUSION

In conclusion, the data obtained from the In-vitro tissue model provides compelling evidence supporting the effectiveness of the implant in mitigating backflow issues. The observed closer proximity of the leaflets confirms the implant's ability to enhance valve function and reduce regurgitation. Moreover, the efficient completion of the procedure within a 45-minute timeframe underscores the practicality and feasibility of the implant in a clinical setting. The significant decrease in leaflet diameter from 38 mm to 30 mm further substantiates the implant's efficacy in promoting improved hemodynamics.

These findings strongly suggest that the implant holds promising potential for addressing backflow complications and ultimately enhancing patient outcomes in real-world scenarios. The results of the In-vitro tissue model presented valuable insights for both preclinical and clinical studies. They serve as a foundation for further investigation and validation through rigorous clinical trials, which will be crucial in establishing the implant's safety and efficacy in a clinical setting. This research work, therefore, acts as a valuable reference for researchers and medical professionals interested in advancing the field of backflow management. Ultimately, this research work has the potential to drive significant advancements in the field, leading to improved patient care and outcomes.

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