Developing Carotid Self-Expanding Stent System for Endovascular Baroreflex Amplification in Hypertension-Induced Heart Failure

Minocha Dr. Pramodkumar, Kothwala Dr. Deveshkumar Mahendralal,

Solanki Himanshu Rajesh and Patel Bhumin Kaushik

Meril Life Sciences Pvt. Ltd., Bilakhia House, Survey No-135/139, Muktanand Marg, Chala, Vapi - 396191, Gujarat, India. E-mail address: mansi.desai@merillife.com

Abstract

Hypertension remains a significant contributor to heart failure, often characterized by increased sympathetic activity through the baroreflex mechanism. In an effort to address this pressing issue, we introduce the 'carotid self-expanding stent system' designed specifically for Endovascular Baroreflex Amplification (EVBA). The primary objective of EVBA is to mitigate hypertension-induced heart failure by modulating sympathetic activity through the baroreflex mechanism. The concept of EVBA involves the precise placement of the carotid self-expanding stent system within the internal carotid artery. This strategically positioned device aims to amplify the baroreflex mechanism, thus counteracting the excessive sympathetic activity responsible for the deterioration of heart failure with decreased ejection fraction. By leveraging this approach, we aspire to achieve a substantial reduction in blood pressure, thereby alleviating the cardiac burden associated with hypertension-induced heart failure. This research article outlines the development and application of the carotid self-expanding stent system for EVBA, offering a comprehensive overview of its mechanism of action, safety profile, and potential therapeutic benefits. Results of in-vitro studies are discussed to elucidate the effectiveness of this groundbreaking intervention in the management of heart failure linked to hypertension. As we delve into the intricacies of this technology, we anticipate that the carotid self-expanding stent system's utilization in EVBA will significantly contribute to the advancement of hypertension management and consequently enhance the quality of life for individuals suffering from heart failure.

Keywords: Hypertension-induced heart failure, Endovascular Baroreflex Amplification (EVBA), Carotid Self-Expanding Stent System, Sympathetic activity modulation, Blood pressure reduction, Heart Failure with Reduced Ejection Fraction (HFrEF)

1. Introduction

Heart failure (HF) is a widespread global health issue, affecting an estimated 26 million individuals worldwide, of which approximately half exhibit reduced ejection fraction, known as HFrEF (Heart Failure with Reduced Ejection Fraction). Remarkable progress has been made in the treatment of HFrEF over recent decades through advancements in pharmacological therapies and the development of devices targeting arrhythmias and secondary mitral regurgitation. These innovations have notably improved the prognosis for many HFrEF patients. However, a significant proportion of individuals with HFrEF continue to experience debilitating symptoms, with more than 30% classified as severely symptomatic (New York Heart Association [NYHA] class III or IV). This subgroup faces compromised quality of life, limited functional capacity, heightened risks of hospitalization, and increased mortality rates. Consequently, HF represents a substantial public health burden, with global expenditures estimated at a staggering $108 billion USD.

In patients with HFrEF, reduced cardiac output and elevated ventricular filling pressures trigger an increase in sympathetic nervous system activity, further exacerbating myocardial oxygen demand and after load. Addressing this autonomic imbalance may hold the key to improving patient outcomes. While beta-blockers have proven effective in reducing sympathetic overdrive and enhancing prognosis, some patients cannot tolerate these medications, and others experience incomplete responses. This has driven exploration into alternative

methods for modulating sympathetic tone in HFrEF patients. One such promising approach involves the stimulation of carotid baroreceptors, resulting in centrally mediated reductions in sympathetic outflow, increased parasympathetic activity, enhanced arterial and venous compliance, and decreased systemic arterial resistance. Baroreflex activation therapy has demonstrated safety and efficacy in HFrEF patients by reducing sympathetic activity.

It is crucial to recognize that baroreceptors respond not to static pressure but to the pulsatile stretching of the carotid sinus wall. Continuous static pressure leads to the resetting of the baroreflex, yielding only transient effects. In contrast, sustained pulsatile pressure results in a more prolonged inhibition of sympathetic activity. With prolonged static pressure exposure, baroreceptor afferent activities adapt over time. However, the adaptation process can be prevented or attenuated if the pressure remains pulsatile rather than static.

The carotid self-expanding stent system is an implant designed to enhance carotid baroreceptor signaling and the baroreflex mechanism. Employing Endovascular Baroreflex Amplification (EVBA), this stent facilitates passive activation of the carotid baroreceptor reflex by altering the geometric shape of the carotid body, thereby increasing carotid sinus wall stretch while preserving pulsatility. This amplified signaling initiates a negative feedback response, leading to a reduction in sympathetic activity and an increase in parasympathetic activity.

This research article seeks to explore the reasons behind creating and employing the carotid self-expanding stent composed of a nitinol alloy as a prospective treatment option for patients with Heart Failure with Reduced Ejection Fraction (HFrEF). It will provide detailed examinations of the safety and effectiveness of this method through in-vitro experiment, offering insights into its ability to restore stable blood pressure and alleviate cardiovascular issues associated with impaired baroreceptor reflexes. Additionally, this research article emphasizes the importance of advancing endovascular procedures to address intricate cardiovascular conditions, with the ultimate goal of improving patient well-being and quality of life.

2. Materials and Method

2.1 Pioneering the Development of Carotid Self-Expanding Stent System Technology:

2.1.1 Precision Engineering: Laser Cutting for Carotid Self-Expanding Stent System Fabrication:

Nitinol, composed of a nickel-titanium alloy, was employed as the material for manufacturing the carotid self-expanding stent system. The design of the stent was created using computer-aided design (CAD) software, encompassing the desired dimensions, patterns, and features of the stent.

The laser cutting machine is equipped with a laser source, focusing optics, a CNC (Computer Numerical Control) system, and a worktable, had been programmed using the CAD design to cut the stent's intricate pattern into the material. The laser beam was precisely focused onto the material's surface and moved along the programmed path. The material was provided in the form of a thin tube or sheet. The laser beam maintained its focus on the material's surface as it moved along the programmed path, cutting out the stent's structure with extreme precision.

2.1.2 Enhancing Surface Precision: Grinding and Honing for Optimization of Carotid Self-Expanding Stent System:

After the implant was shaped through laser cutting, it often exhibited surface irregularities, including minor burns, rough edges, and residual material from the original tube. These imperfections had the potential to adversely affect the implant's performance and biocompatibility. To address this issue, a grinding and honing process was conducted.

Grinding entailed the use of abrasive materials, such as grinding wheels or belts, to eliminate undesired material from the implant's surface. This process could be automated to ensure consistent and precise results, effectively eliminating rough edges and any excess material left from the laser cutting process.

Subsequently, the honing process was employed, involving the use of abrasive stones or tools to create a fine, smooth, and uniformly polished surface. This meticulous approach enhanced the implant's surface precision.

Both grinding and honing, which could be automated using well known machines, played a crucial role in ensuring the biocompatibility of the implant. They would minimize the risk of tissue irritation or damage when the implant will be inserted into the body, enhancing its overall performance and safety.

2.1.3 Harnessing Shape Memory in Nitinol for Manufacturing Carotid Self-Expanding Stent System:

The nitinol implant was shaped into the desired form using a shape-setting process, where a mandrel, typically composed of heat-resistant material, served as a template. The nitinol component was placed onto the mandrel or fixture to ensure complete contact with its surface. Subsequently, the assembly was heated to a precise temperature. Nitinol possesses a distinctive attribute known as shape memory, enabling it to retain a specific shape set at a particular temperature. Upon reaching the critical temperature, heat facilitated the nitinol's return to the predetermined shape.

2.1.4 Addressing Imperfections in Carotid Self-Expanding Stent System through Sandblasting:

Sandblasting is a crucial post-shape-setting step in biomedical applications aimed at achieving a uniform, high-quality surface finish. Despite precise shape settings, microscopic imperfections, irregularities, and contaminants could remain on the implant's surface, including tiny burrs, residual material, or uneven textures. Sandblasting used abrasive particles like aluminum oxide to address these issues. Its objectives included minimizing corrosion risk, reducing bacterial adhesion and biofilm formation, promoting biocompatibility, and enhancing aesthetic appearance.

2.1.5 Enhancing Carotid Self-Expanding Stent System through Electro-Polishing:

Electro-polishing was employed to eliminate residual imperfections and improve the implant's surface. This electro-chemical process dissolved surface material in an electrolyte solution, effectively removing contaminants, edges, and burrs. The implant was immersed in the electrolyte solution, and an electric current was applied, causing metal ions from the surface to dissolve into the solution. This resulted in a smoother and uniform surface of carotid self-expanding stent system by leveling and eliminating sharp or uneven features. The resulting assembly is depicted in the **figure.01.** The implant is available in 3 sizes: A) vessel diameter 5.00-7.00 mm, B) 6.25-9.00 mm, and C) 8.00-11.75 mm and the length ranges from 25 - 35 mm.

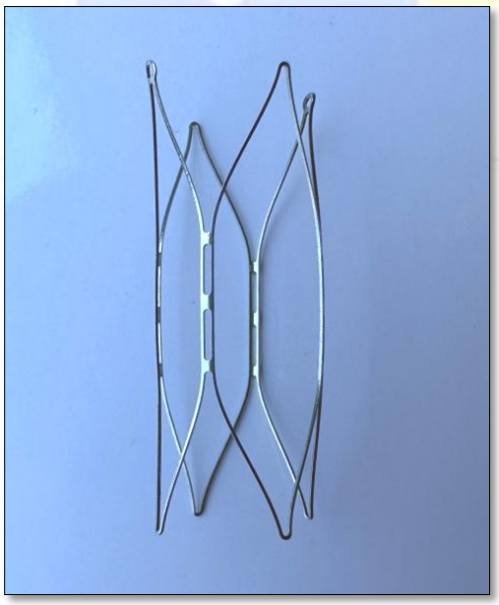

Figure.01 Exploring the carotid self-expanding stent from diverse perspectives

3. The Delivery System

The delivery system shown in the **figure.02** plays a pivotal role in the precise and safe placement of stents within the carotid body. Here's a detailed breakdown of the process:

3.1 Components of the Delivery System:

1. Soft Tip: The soft, flexible front end of the catheter, easing its insertion and movement within the body.

2. Catheter: A thin, flexible tube serving as a conduit for transporting the stent to the target location. 6Fr catheter is used to deploy the stent.

3. Inner Lumen: A hollow channel within the catheter, facilitating stent passage and deployment.

4. Handle: The part used by medical professionals to manipulate the catheter.

5. Thumbwheel: A control mechanism on the handle, enabling the user to manage stent deployment.

6. Hub: The Hub is used for flushing the guidewire port and priming purposes too.

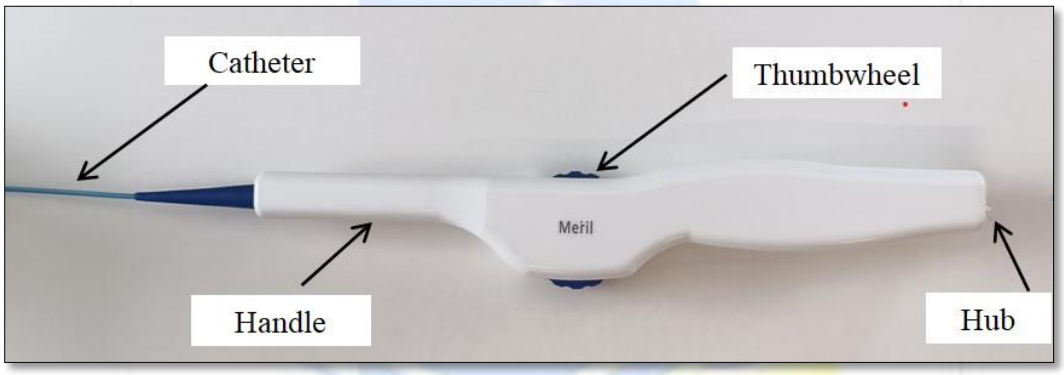

Figure.02 The ingenious conduit for deploying the carotid self-expanding stent

3.2 Construction of the Delivery System: The delivery system is meticulously designed and constructed, balancing flexibility and stability. This design allows for smooth maneuverability within the body while minimizing the risk of implant's damage during insertion and deployment.

3.3 Mechanism of the Delivery System: The delivery system is engineered to be user-friendly. Its primary function involves controlled stent release from the catheter at the target location.

3.4 Procedure for Deploying the Stent:

a. Catheter Insertion: The process initiates by inserting the catheter into the patient's body, typically through a specific access point like the femoral artery, chosen based on the stent's target location.

b. Guide wire Assistance: To precisely guide the catheter within the body, a guidewire is often employed. This guidewire is inserted through the catheter, aiding navigation to the desired region.

c. Fluoroscopy for Visualization: Fluoroscopy, an X-ray-based real-time imaging technique, is frequently used during the procedure to verify accurate catheter positioning at the desired location.

d. Stent Deployment: After the catheter is correctly positioned, stent deployment commences. This process is controlled by rotating the thumbwheel on the handle, regulating stent movement through the catheter's inner lumen. The rotation speed and extent depend on the stent's length and specific procedure requirements. The partial stent deployment is depicted in the **figure.03**

e. Fluoroscopy for Confirmation: Fluoroscopy continues to be employed throughout stent deployment to monitor progress and confirm precise stent placement.

3.5 Completion of Stent Deployment: The entire stent deployment process is meticulously monitored via fluoroscopy. Once it is confirmed that the stent is accurately positioned at the target location, the deployment process is concluded.

Figure.03 The partial deployment of a carotid self-expanding stent

4. Results and Discussion

In a recent research study, we utilized a carotid self-expanding stent system along with its delivery system as an endovascular implant to enhance circumferential and longitudinal wall strain at the level of the carotid baroreceptors. This innovative approach holds the potential to activate the baroreflex and consequently reduce blood pressure. The experiments involved the in-vitro implantation of the carotid self-expanding stent using the specified delivery system, all within a simulated vasculature model designed to replicate conditions encountered in the human carotid artery (in-vivo).

The delivery system, including the loaded implant, proved to be remarkably straightforward and user-friendly for deploying the stent at a precise location, known as the targeted site. During the implantation procedure, the catheter was carefully introduced into the simulated vasculature model, as illustrated in the **figure.04**

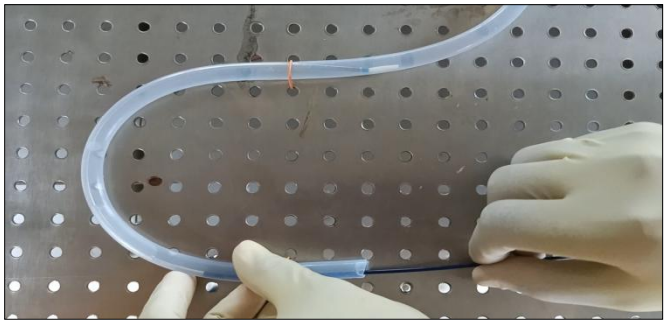

Figure.04: Simulation vasculature model illustrating the intricacies of a vascular system simulation.

It was then navigated to the intended site within the simulated vascular model as shown in the **figure.05**, which corresponded to where the implant was expected to be deployed. This precise navigation was achieved by rotating a thumb wheel, which allowed for the controlled deployment of the stent inside the model at the desired location. Upon deployment, the stent, which had been crimped, regained its original shape, as depicted in the **figure.06.** This ability of the stent to return to its initial configuration ensured that the carotid self-expanding stent system was appropriately positioned within the simulated vasculature model at the targeted site.

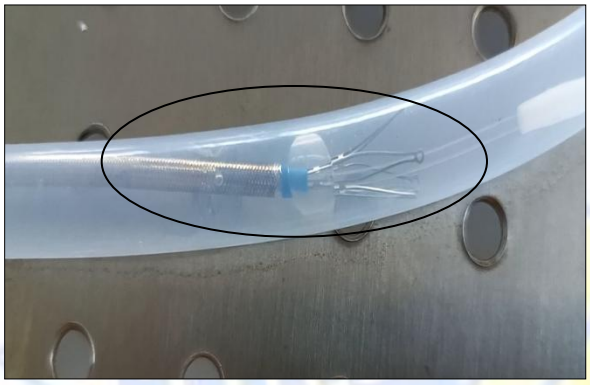

Figure.05 An illustrative portrayal of the stent deployment process.

Furthermore, the delivery components of the system endowed it with enhanced flexibility and lubricity, facilitating smooth movement through the intricate pathways of the vasculature. Consequently, the friction encountered during delivery was significantly reduced compared to conventional delivery systems.

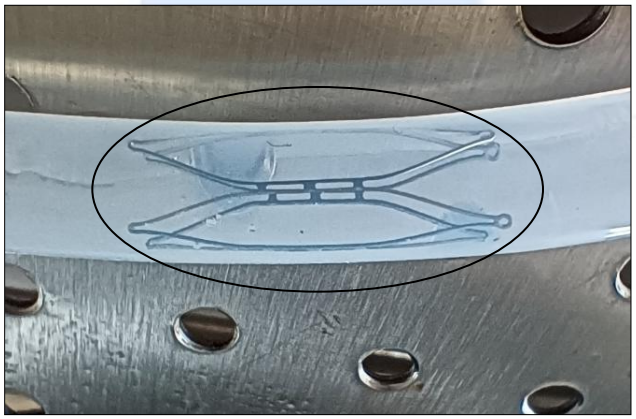

Figure.06 The implant returning to its original shape after the deployment procedure.

In summary, the results obtained from the in-vitro implantation of the carotid self-expanding stent system using the provided delivery system within the simulated vasculature model unequivocally demonstrated its effectiveness and potential for enhancing endovascular interventions. These findings would lend strong support to its use as a viable option for achieving successful implantation when applied in-vivo within the carotid artery. The traditional/conventional design's disadvantage is that it limits the blood flow to an additional artery. Unlike the previous innovation, the stent design of the current invention does not impede the blood flow to another artery. On the other hand, the recently developed carotid stent device used in the in-vitro implantation trial has yielded encouraging results.

5. Conclusion

The research study underscores the potential of endoscopic carotid self-expanding stent system as a vital treatment for resistant hypertension. Its strengths lie in the rapid deployment mechanism, cost-effectiveness, and safety demonstrated within a vasculature simulation model. This breakthrough offers promise in tackling resistant hypertension and reducing the incidence of heart failure, a dire consequence of uncontrolled hypertension. The study's implications are significant, enhancing our understanding of resistant hypertension treatment and opening doors for future pre-clinical investigations. Integrating the aforementioned implant with delivery system into clinical practice has the potential to revolutionize treatment strategies and improve long-term patient outcomes. However, it's crucial to acknowledge that this research represents a preliminary step in effectively addressing resistant hypertension. Further studies and extensive clinical trials are essential to validate and expand on these promising findings. These future endeavors should focus on refining and customizing the endoscopic carotid self-expanding stent system placement for patients with heart failure and reduced ejection fraction. This tailored approach aims to provide more effective and targeted treatment options, ultimately enhancing the lives of those dealing with this challenging medical condition.

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