ONLINE SUPPLEMENTAL MATERIALS

Novel Mechanical Thrombectomy System for the Treatment of Intermediate-Risk Acute Pulmonary Embolism: A Prospective Multicenter Study

Running title: Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism

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SUPPLEMENTAL METHODS

ANIMALS AND TREATMENT. The study was performed by PharmaLegacy (Shanghai, China) and received local ethics approval. The study complied with the National Institutes of Health Guide for the Care and Use of Laboratory Animals. All white domestic pigs weighed around 40 kg and were housed at a temperature of 16°C–26°C and a humidity of 40%–70% under a constant 12-hour light/12-hour dark cycle. The experimental animals were administered standard pelleted feed. The experimental animals had ad libitum access to drinking water throughout the experiment, which was purified, filtered, and sterilized by the reverse osmosis system at the experimental institution.

Blood was collected from the animals for clinical pathological examination. All measured indicators were within normal ranges, suggesting that the animals were in good health before the procedure and during material collection, and that the procedure did not have adverse effects on the experimental animals.

SAFETY EXPERIMENT. First, the safety of the Tendvia system (Tendfo Medical, Shanghai, China) was evaluated in a porcine model without pulmonary embolism. The femoral vein was punctured to establish vascular access. Pulmonary branch angiography was performed to prepare for the subsequent thrombus to stay at the target location and to measure the target vessel size (Supplemental Figure 1a–i). To establish the pathway to introduce the instrument, the introduction sheath of the corresponding specification was placed. The aspiration catheter was passed through the introduction sheath and sent to the target vessel through the guidewire, after which the dilator in the aspiration catheter was removed. The Tendvia system was delivered along the guidewire through the aspiration catheter to the target vessel. To release the Tendvia clot retrieval catheter, the disks were released and left in place for approximately 5 minutes to simulate full self-expansion of the disks.

To mimic mechanical thrombectomy, the 60 mL syringe was connected to the aspiration catheter infusion tube, and after the connector was closed, the syringe was drawn to the 60 mL mark and locked. The pushing tube was pulled back to recover the disks into the aspiration catheter, and the connector was opened to apply suction to the aspiration catheter. After the disks had completely entered the aspiration catheter, the Tendvia clot retrieval catheter was withdrawn from the body. The guidewire in the aspiration catheter was removed, and the tail end of the catheter was sealed. The 60 mL syringe was connected to the infusion tube connector at the tail end of the aspiration catheter, and after the infusion tube connector was closed, the syringe was drawn to the 60 mL mark and locked.

To mimic thrombus aspiration, the infusion tube connector was opened, and aspiration was performed once. After the completion of aspiration, the aspiration catheter was withdrawn from the body. The wound was treated at the end of the procedure.

EFFECTIVENESS EXPERIMENT. Next, we investigated the effectiveness of the Tendvia system in a porcine model with pulmonary embolism. Before thrombus injection, epinephrine (1 mL dissolved in 50 mL saline; pump flow rate of 5 mL/hour) was administered prophylactically. If breathing and cardiac arrest occurred after modeling, cardiopulmonary resuscitation was performed immediately. To establish the model of vascular thromboembolism, an introduction sheath of the corresponding specification was used to inject the thrombus into the pulmonary artery branch and maintain it within the branch. The presence of thromboembolism was confirmed by angiography.

To establish the pathway to introduce the instrument, the guidewire was passed through the thrombus site for at least 5 cm. The aspiration catheter was brought to the proximal end of the thrombus through the guidewire, and the port of the aspiration catheter was located at the proximal end of the thrombus through the radiographic aid device. The Tendvia clot retrieval catheter was delivered along the guidewire through the aspiration catheter to the thrombus,

and radiation-assisted positioning was used to ensure that the conical head of the device passed the thrombus and reached the distal end of the thrombus. This was to ensure that the thrombus was located in the disks and that the development point of the proximal end of the device was greater than the development point of the distal end of the aspiration catheter. The Tendvia clot retrieval catheter disks were released and placed at rest at the thrombus location for a sufficient time (approximately 5 minutes) to enable full expansion of the disks for thrombus embedding.

For mechanical thrombectomy, a 60 mL syringe was connected to the infusion tube connector at the tail end of the aspiration catheter, and after the infusion tube connector was closed, the syringe was drawn to the 60 mL mark and locked. As the pushing tube was pulled back to retrieve the disks into the aspiration catheter, the infusion tube connector was opened to apply suction to the aspiration catheter. After the basket had completely entered the aspiration catheter, the Tendvia clot retrieval catheter was withdrawn from the body. For preparation before aspiration alone, the guidewire in the aspiration catheter was removed, and the tail end of the catheter was sealed. After connecting the 60 mL syringe to the infusion tube connector at the tail end of the catheter and closing the connector, the syringe was drawn to the 60 mL mark and locked. For thrombus aspiration alone, the connector was opened, and aspiration was performed once. After confirming that the thrombus was removed, target vessel recanalization after thrombectomy was evaluated by angiography. If angiography showed that recanalization of the target site was satisfactory, the aspiration catheter was removed to end the procedure. If angiography revealed that there was still residual thrombus at the target site of thrombectomy, the thrombus removal basket and the lumen of the aspiration catheter were washed with physiological saline, and the above steps were repeated to remove the remaining thrombus. If the thrombus could not be washed away, the system was replaced to remove the thrombus again. A maximum of two thrombectomy procedures

were performed for each set of instruments, and no more than four thrombectomy procedures were performed for each vessel.

POSTOPERATIVE CARE. After the procedure and after recovering from anesthesia, the experimental animals were transferred to the animal room to undergo observation and feeding. During the postoperative observation period, the animal care standards were followed to manage and maintain the animal temperature within the normal range, reduce pain and infection, and provide sufficient water and electrolytes. Postoperative care and medication information were recorded on the corresponding forms.

The health status of the experimental animals was comprehensively assessed twice per day by a veterinarian. The data collected included the mental state, physical condition, and locomotor activity of the animals. The results of the detailed daily observations were recorded on the corresponding forms.

The veterinarian recorded and notified the experimenter in charge of any abnormalities or adverse events that may be related to the device, as well as any abnormalities or adverse events that may affect the integrity of the experiment.

The animals were bred until the expected endpoint was reached. The animals were euthanized after the end of follow-up.

PATHOLOGICAL ANALYSIS. Animals were euthanized according to the plan and autopsied. The chest was opened, the test site was observed, and images were taken (the images were marked with at least the experiment number, animal number, and collection time) to observe whether there were any abnormalities.

After the above procedures were completed, a comprehensive gross autopsy was performed on the other tissues and major organs. The heart, liver, spleen, lungs, brain, and kidneys were removed, and the infarction lesions and other abnormalities were grossly observed. The images were marked with at least the experiment number and animal number.

Dissection of the experimental animals was recorded on the animal experiment record form. Any anomalies were described in detail and recorded. Photographs were required during autopsy to supplement the anatomical records.

The tissues collected from the blood vessel segments that were subjected to thrombectomy were stored in 10% neutral formalin fixative solution for a minimum of 48 hours. After alcohol gradient dehydration, the tissues were cleared in xylene, three thrombectomy segments were removed, and two blank blood vessels on the other side of the segment were used as controls (Supplemental Figure 2). These vessels were subsequently embedded in paraffin and sectioned laterally.

The harvested hearts, liver, spleen, lungs, and kidneys were preserved in 10% neutral formalin fixative for a minimum of 48 hours. After alcohol gradient dehydration, the tissues were cleared in xylene, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Histopathological evaluation was performed. Pathological analysis of major organs was not performed in the acute experiments.

The experiment required a Quality Assurance audit, and all experimental processes were executed in strict accordance with the corresponding standard operating procedures and/or experimental protocols. The experimental report was sent to the project sponsor for review before finalization.

SUPPLEMENTAL RESULTS

A total of 12 white domestic pigs were included in the experiment. Six of the animals were dissected immediately after completion of the experiment (immediate group), while the other six were followed up for 30 days after wound closure (the 30-day group).

We found that the Tendvia system could be used to perform thrombectomy and simulated thrombectomy in all animals with good operability. During thrombectomy, the pulmonary thrombectomy system was able to open the test segment of the pulmonary artery

and restore blood flow in the animal model of thromboembolism (Supplemental Figure 3a & b), indicating the effectiveness of this system for thrombectomy. No abnormalities or adverse surgical complications occurred with the pulmonary thrombectomy system during simulated thrombectomy or thrombectomy. The experimental animals reared under observation showed no abnormal clinical manifestations in the feeding stage, and no abnormalities were found at follow-up or on gross anatomical analysis. The histopathological analysis revealed no vascular perforation, dissection, or hematoma in the pulmonary artery. Pathological analysis (Supplemental Figure 4a & b) of the test segment revealed that the pulmonary artery site in the immediate group and 30-day group had no obvious perforation, dissection, or hematoma compared with the blank control group.

SUPPLEMENTAL TABLES

SUPPLEMENTAL TABLE 1 Quantitative Vessel Analysis in the Immediate Group

Animal ID	Blood Vessel Test	Vessel MLD of Test Segment Before Test (mm)	Vessel MLD of Test Segment After Test (mm)	Evaluation of the Effect of Thrombectomy for the Test Vessel Segment
P00312	Left pulmonary artery	8.4	5.2	Success
P00313	Left pulmonary artery	10.7	9.5	Success
P00314	Left pulmonary artery	10.5	4.7	Success
P00315	Left pulmonary artery	9.2	7.0	Success
P00316	Left pulmonary artery	9.0	5.5	Success
P00308	Left pulmonary artery	12.7	8.2	Success
Mean Value		10.1	6.7	---
Standard Deviation		1.4	1.7	---

MLD, minimum lumen diameter.

SUPPLEMENTAL TABLE 2 Quantitative Vessel Analysis in the 30-Day Group

Animal ID	Blood Vessel Test	Vessel MLD of Test Segment Before Test (mm)	Vessel MLD of Test Segment After Test (mm)	MLD (Mm) At 30-Day Follow-Up	Percent Stenosis (%)
P00283	Right pulmonary artery	11.9	11.9	12.5	−5.0
P00284	Left pulmonary artery	12.1	11.2	11.7	−4.5
P00285	Left pulmonary artery	8.8	9.6	9.9	−3.1
P00286	Left pulmonary artery	12.5	13.5	10.4	23.0
P00287	Right pulmonary artery	11.2	11.1	11.4	−2.7
P00288	Right pulmonary artery	12.5	13.2	11.7	11.4
Mean Value		11.5	11.8	11.3	3.2
Standard Deviation		1.3	1.3	0.9	10.5
***P* value (pretest/at the time of follow-up)**				0.572	

MLD, minimum lumen diameter.

SUPPLEMENTAL FIGURE LEGENDS

SUPPLEMENTAL FIGURE 1 Workflow of the Preclinical Animal Study Using the Tendvia System

a) The pulmonary artery before the Tendvia system was tested. **b**) Pulmonary artery thrombosis was modeled. **c**) The Tendvia system reaching the target location for the first time during thrombectomy. **d**) The Tendvia system at the first deployment. **e**) The Tendvia system when it was withdrawn for the first time. **f**) The Tendvia system reaching the target position for the second time. **g**) The Tendvia system at the second deployment during the thrombectomy procedure. **h**) The Tendvia system when it was withdrawn for the second time. **i**) Thrombus removal.

SUPPLEMENTAL FIGURE 2 Schematic of Blood Vessel Sections

A, **B**, and **C** are the thrombectomy segments, while **d** and **f** are the blank vascular segments.

SUPPLEMENTAL FIGURE 3 Demonstration of Effective Thrombectomy

a) The pulmonary artery was blocked by a thrombus. **b**) The pulmonary artery thrombus was removed and blood flow restored.

SUPPLEMENTAL FIGURE 4 Pathological Analysis of the Pulmonary Artery

a) No obvious vascular injury was observed in the blank group (the contralateral unmanipulated vessel). **b**) In the thrombectomy group, no vascular perforation, dissection, or hematoma was observed.

SUPPLEMENTAL VIDEO LEGEND

SUPPLEMENTAL VIDEO 1 Demonstration of the Tendvia System for Mechanical Thrombectomy in the Treatment of Acute Pulmonary Embolism