Management of Complicated Aortic Aneurysms Using Multiple Overlapping Uncovered Stents

Mid-Term Outcome From a Cohort Study

Yongxue Zhang, MD, Zhongzhao Teng, PhD, Qingsheng Lu, MD, Zhiqing Zhao, MD, Junmin Bao, MD, Xiang Feng, MD, Rui Feng, MD, Zengsheng Chen, PhD, Yuan Huang, PhD, Umar Sadat, MD, Jonathan H Gillard, MD, and Zaiping Jing, MD

Abstract: This study sought to report the mid-term outcome of a modified flow-diverting strategy in the treatment of complicated aortic aneurysms of different morphology.

Historical data suggested aortic aneurysm expansion and rupture after endovascular treatment with current commercial flow-diverters, indicating the essentiality of further investigation of this technique prior to its large-scale clinical application.

An alternative flow-diverting strategy using layer-by-layer assembled multiple overlapping uncovered stents was employed in this study. The treatment outcome in aneurysms of different morphology (saccular, fusiform, and dissecting) was assessed during a mid-term follow-up period.

Of 42 patients enrolled in this study (30 male, mean age: 63.3 years), technical success was achieved in 40 cases. During an average follow-up period of 20.9 months, mean aneurysm diameter shrunk from 53.4 ± 13.6 mm to 48.8 ± 13.9 mm (P < 0.001), while stent-induced sac thrombosis ratio increased significantly ($18.1 \pm 14.9\%$ to $93.6 \pm 9.5\%$, P < 0.001). The majority of side branches (74/76 major visceral branches, 237/244 minor segmental arteries), covered by 3.3 stents on average, maintained their patency after stenting. Saccular aneurysm manifested the highest thrombus deposition speed (18/20 were totally thrombosed within 12 months) and most significant shrinkage (51.4 ± 13.3 mm pre-operatively vs

Yongxue Zhang and Zhongzhao Teng contributed equally to this work.

Funding sources: This research project is financed by the following public foundations: National Nature Science Foundation of China (81170291, 39800177, and 30772140), British Heart Foundation (PG/11/74/29100), and Chinese Scholarship Council (201306580020).

None of the authors has a conflict of interest to disclose

Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins. This is an open access article distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0, where it is permissible to download, share and reproduce the work in any medium, provided it is properly cited. The work cannot be changed in any way or used commercially.

ISSN: 0025-7974

DOI: 10.1097/MD.000000000000209

 43.5 ± 10.2 mm during follow-up, P < 0.001) compared with fusiform and dissecting aneurysms.

This modified flow-diverting strategy could be a feasible alternative in the management of complicated aortic aneurysms where vital branches need to be preserved. The treatment outcome may depend on the aneurysm type. Further studies with larger patient cohort and longer follow-up are required to substantiate these results.

(Medicine 93(27):e209)

Abbreviations: CMS = cardiatis multilayer stent, CTA = computed tomography angiography, D-An = dissecting aneurysm, F-An = fusiform aneurysm, MOUS = multiple overlapping uncovered stents, RA = renal artery, SA = segmental artery, S-An = saccular aneurysm, SCI = spinal cord ischemia, STR = Sac thrombosis ratio.

INTRODUCTION

The concept of flow-diverting stents was first described nearly two decades ago, when Geremia et al¹ suggested that a low-mesh-porosity metallic stent bridging an aneurysm would alter the local flow pattern, promoting thrombus formation and thereby theoretically leading to aneurysm exclusion. Validation of this theory in intracranial and peripheral aneurysms has proven its potential in terms of aneurysm exclusion and collateral branches' preservation.^{2,3}

When it comes to aortic pathologies, on the other hand, serious concern has been raised regarding the flow diverters' efficacy. Aneurysm expansion and rupture after stenting have been reported^{4–6}; significant stent longitudinal shortening during its deployment could lead to insufficient coverage of the aneurysm⁷; and when 2 or more stents are required, the overlapping zone might be too rigid to accommodate the degree of aortic angulation, leading to a potential risk of aortic rupture.⁸ However, given their unique advantage in preserving side branches,^{3,6,7} the translational application of flow-diverting stents should not be discouraged by these adverse reports. In most reported studies,^{3–8} cardiatis multilayer stent

In most reported studies,^{5–6} cardiatis multilayer stent (CMS, Cardiatis, Isnes, Belgium) was used. This highly deformable stent may shorten and migrate from the original target location after deployment, possibly resulting from inadequate stent overlap or use of an undersized device; moreover, its configuration is pre-defined and therefore this system lacks of the flexibility of being adjusted for the individual patient. In our center, an alternative protocol using multiple overlapping uncovered stents (MOUS, Sinus-XL stent, OptiMed, Ettlingen, Germany) has been proposed aiming at overcoming these limitations. The short-term outcome was encouraging,⁹ but the conclusion was limited by the relatively small study series and short follow-up length. Moreover, the treatment outcome

Editor: Dai Yamanouchi.

Received: June 25, 2014; revised: September 30, 2014; accepted: October 6, 2014.

From the Division of Vascular Surgery, Changhai Hospital, Shanghai, China (YZ, QL, ZZ, JB, XF, RF); University Department of Radiology, University of Cambridge, UK (YZ, ZT, YH, JHG); Department of Engineering, University of Cambridge, UK (ZT); School of Aerospace, Tsinghua University, Beijing, China (ZC); Cambridge Vascular Unit, Addenbrooke's Hospital, Cambridge, UK (US); and Military Institute of Vascular Disease, the First Affiliated Hospital of Second Military Medical University, Shanghai, China (ZJ).

Correspondence: Qingsheng Lu, Division of Vascular Surgery, Changhai Hospital, 168 Changhai Road, 200433, Shanghai, China (e-mail: luqs@xueguan.net) or Prof Zaiping Jing, Military Institute of Vascular Disease, The First Affiliated Hospital of the Second Military Medical University, 168 Changhai Road, 200433, Shanghai, China (e-mail: jingzp@xueguan.net).

may also depend on the aneurysm morphology,³ which has been least investigated in the literature.

The present study focuses on exploring the impact of aneurysm morphology on the treatment outcome after the MOUS procedure in a larger patient cohort with mid-term follow-up, and providing initial evidences for future patient selection and post-operative management.

METHODS

This study was approved by the review board of Changhai Hospital and written informed consent was obtained from each patient.

Patient enrolment was based on consensus from a multidisciplinary surgical team consisting of vascular surgeons, cardio-thoracic surgeons, and anesthetists based on the following criteria:

- 1 Diagnosis of aortic aneurysms by computed tomography angiography (CTA); with an aneurysm neck \leq 30 mm.
- 2 Patient judged inappropriate for open surgical repair according to the following standard: American Society of Anesthesiologists classification \geq IV, New York Heart Association classification (1994) of cardiac function of \geq III/C, or dysfunction of other important organ systems (such as severe chronic obstructive pulmonary disease, renal or hepatic insufficiency).¹⁰
- 3 Vital branches involved, including major branches such as the superior mesenteric artery, celiac artery, and renal arteries (RA), and minor branches such as the segmental arteries (SA) in patients judged at an high risk of spinal cord ischemia (SCI) according to the reported risk factors, including anticipated endograft coverage of distal descending aorta up to T8-L1 level, where the segmental artery most frequently feeds the Adamkiewicz artery^{11,12}; planned long extent coverage of aorta more than 205 mm¹³; planned sacrifice of the left subclavian artery without revascularization (due to the risk of general anesthesia and open procedure)¹⁴; or already compromised collateral network of

spinal cord blood supply (ie, previous infrarenal aortic aneurysm repair with occluded hypogastric arteries).¹⁵

Pre- and Post-Operative Imaging

All patients enrolled in this study were examined by CTA on a multi-slice CT scanner (Sensation Cardiac 64, Siemens, Germany) before the MOUS procedure and during the followup. To assess the major branches as well as the small SAs arising from the aorta, the CT slice thickness was set to be 1 mm. CTimage processing software (Aquarius Workstation, TeraRecon, Inc.) was used for 3-dimensional reconstruction of the aortic contour and parameter measurement. Pre- and post-operative CT images were co-registered referring to the vertebrae. Maximum aneurysm diameter was measured on the cross-sectional image (Figure 1). Sac thrombosis ratio (STR) was defined as the percentage of thrombus volume to the whole sac volume (Figure 2). The number of branches within the anticipated coverage zone was recorded before surgery, and the patency of each was assessed during follow-up (Figures 1 and 2). All measurements were made by the first author and verified independently by two co-authors.

Intervention Procedures

The stents inserted in this study were closed-cell, selfexpandable uncovered stents (OptiMed, Ettlingen, Germany). The distribution of the overall stent mesh porosity when different layers were placed together in a random pattern was studied via computational simulation (*please refer to text document*, *Supplemental Digital*, http://links.lww.com/MD/A88, *which describes the detailed simulation process and results*).

Under local anesthesia, the femoral arteries were punctured followed by 8 Fr sheaths (Medtronic, Minneapolis, MN) insertion, with heparin given intra-arterially (80 IU/kg). An angiogram was performed via a 6 Fr pigtail catheter (Medtronic) to confirm the size and location of the aneurysm. The sheath was then replaced by a larger one (10 Fr). An extra-stiff guidewire



FIGURE 1. Assessment of aneurysm evolution with computed tomography angiography (CTA). (A) Pre-operative CTA demonstrated the aneurysm was located at the level of T8 to T10 level of aorta. Segmental arteries within the anticipated cover zone were noted (*white arrow heads*). (B and C) The maximum diameter of the aneurysm before and after intervention was measured on the cross-sectional image of the same aortic level, using the vertebrae as markers. (D and E) Each segmental artery noted before stenting was evaluated during follow-up to document its patency (*black arrows*). (F) At 6 months, the aneurysm sac was totally thrombosed, leaving all segmental arteries patent (*white arrow heads*). L stands for the arterial lumen and S for aneurysm sac.



FIGURE 2. Calculation of sac thrombosis ratio. (A) A saccular aneurysm was found at T11 to L1 aortic level. Segmental arteries (SAs) covered were marked (*white arrow heads*). (B) At 12 months, the aneurysm was partially thrombosed, and the SAs maintained their patency (*white arrows*). (C and D) The areas of the thrombus and the residual perfusion were measured on the cross-sectional images by changing the window level to get the optimal view of each tissue (the thrombus was marked by *white asterisk* in C and the residual perfusion was marked by *white asterisk* in C and the residual perfusion was marked by *black asterisk* in D). Aneurysm sac thrombosis ratio (STR) was defined as the total thrombus volume over the whole aneurysm sac volume, and was calculated from the following formula: $STR = \sum (A_{thrombus} \times ST) / \sum (A_{sac} \times ST)$, where $A_{sac} = A_{thrombus} + A_{rp}$. In which STR stands for the sac thrombosis ratio, $A_{thrombus}$, A_{rp} , and A_{sac} stand for the area of thrombus, residual perfusion, and the whole sac on the cross-sectional images, respectively; and ST stands for the slice thickness of the scan protocol.

(Cook, Bloomington, IN) was placed to bridge the diseased segment of aorta, following which the stents were advanced and deployed consecutively from proximal to distal to cover the aneurysm. There was at least 15 mm of lesion-free landing zone at the proximal and distal aortic neck. The diameter of the stents conformed to manufacturer's instruction, with 10% to 20% oversizing at the aneurysm neck. The number of stents implanted was determined by intra-operative angiography with the criterion that a significant decrease of flow velocity in the aneurysm sac was achieved on fluoroscopy (*see videos, Supplemental Digital*, http://links.lww.com/MD/A89 *amd* http://links.lww.com/MD/A90, *which show the local flow velocity change within the aneurysm sac after 1 and 3 stents were deployed, respectively*). Side branches, including SAs and visceral branches, were covered wherever necessary.

Aneurysm sac pressure was monitored in 19 patients to document its change before and after stenting (*see text document, Supplemental Digital,* http://links.lww.com/MD/A91, which describes the pressure measurement and calculation procedure in detail). Technical success was defined as successful deployment of the stents to target locations without procedure-related complications, conversion to open surgery, or perioperative mortality.¹⁶

Clinical and Imaging Follow-Up

All patients were discharged with strict blood pressure control (\leq 120/80 mm Hg). The evolution of each aneurysm was followed up using CTA firstly at 3 and 6 months, then every

6 months onwards. Telephone interview was performed monthly. The treatment outcome was partially assessed by the change of aneurysm maximum diameter: the change in maximum diameter <5 mm was considered as non-significant; and a reduction and growth by more than 5 mm in diameter were defined as aneurysm shrinkage and expansion, respectively. Clinical success was defined as complete shrinkage or stabilization of an aneurysm without major complications (including symptomatic visceral ischemia due to branch occlusion, SCI, stent thrombosis or infection, aneurysm-related mortality etc.).¹⁶

Statistical Analysis

All analyses were based on the intend-to-treat principle. The Kolmogorov–Smirnov method was used to assess the distribution of continuous parameters. Two-tailed Student's *t*-test was used if a normal distribution was observed; otherwise non-parametric two-tailed Mann–Whitney test was performed. Kaplan–Meier method was used to analyze the survival rate and the cumulative percentage of patients whose aneurysm sac was patent with residual perfusion during follow-up. Statistical significance was assumed if P < 0.05. SPSS 13.0 (SPSS, Inc., Chicago) was used for the statistical analysis.

RESULTS

Between March 2010 and February 2013, a total of 42 patients were enrolled in this study with 21 (50%) saccular aneurysms, 8 (19%) fusiform aneurysms, and 13 (31%) aortic dissections. Patient demographics are listed in Table 1.

Variables	Overall	S-An	F-An	D-An
Demographics				
No. of patients	42	21	8	13
Male	30 (71.4%)	15 (71.4%)	5 (62.5%)	10 (76.9%)
Age (vears)	63.3 ± 14.6	61.4 ± 16.3	73.1 ± 10.7	60.2 ± 11.5
Risk of open surgery				
Elderly $(>70 \text{ years})$	16 (38.1%)	7 (33.3%)	5 (62.5%)	4 (30.8%)
COPD	14 (33.3%)	6 (28.6%)	4 (50.0%)	4 (30.8%)
Cardiac failure	11 (26.2%)	6 (28.6%)	2 (25.0%)	3 (23.1%)
Renal insufficiency	9 (21.4%)	4 (19.0%)	4 (50.0%)	1 (7.7%)
Liver failure	5 (11.9%)	3 (14.3%)	2 (25.0%)	0 (0)
Ischemic stroke	4 (9.5%)	1 (4.8%)	2 (25.0%)	1 (7.7%)
Others*	2 (4.8%)	2 (9.5%)	0 (0)	0 (0)
Location of the aneurysms				
Thoracic	15 (35.7%)	7 (33.3%)	0 (0)	8 (61.5%)
Thoracoabdominal	8 (19.0%)	2 (9.5%)	6 (75.0%)	0 (0)
Pararenal abdominal	14 (33.3%)	9 (42.9%)	1 (12.5%)	4 (30.8%)
Juxtarenal abdominal	5 (11.9%)	3 (14.3%)	1 (12.5%)	1 (7.7%)
Side branches involved (Patent/cove	red)			
Celiac artery	20/20	8/8	7/7	5/5
Superior mesenteric artery	21/21	10/10	7/7	4/4
Renal artery	33/35	14/15	15/16	4/4
Segmental artery	237/244	118/121	41/43	78/80
Procedural details				
Procedure time (min)	64.2 ± 28.5	54.8 ± 24.6	90.0 ± 21.4	63.5 ± 30.2
X-ray exposure time (min)	31.8 ± 12.6	28.6 ± 11.0	38.1 ± 12.2	33.1 ± 14.4
Contrast media dose (mL)	98.1 ± 29.9	88.6 ± 25.0	122.5 ± 40.6	98.5 ± 22.3
No. of stents deployed	3.3 ± 1.0	3.1 ± 0.7	4.0 ± 1.4	3.0 ± 0.9
Hospital stay (days)	8.6 ± 4.0	8.9 ± 5.0	9.8 ± 2.6	7.4 ± 2.5
Post-operative events				
Follow-up (month)	20.9 ± 9.0	23.2 ± 10.4	15.3 ± 3.6	20.8 ± 7.8
In-hospital complications	3 (7.1%)	1 (4.8%)	0 (0)	2 (15.4%)
In-hospital mortality	1 (2.4%)	1 (4.8%)	0 (0)	0 (0)
Follow-up complications	0 (0)	0 (0)	0 (0)	0 (0)
Follow-up mortality	1 (2.4%)	0 (0)	1 (12.5%)	0 (0)

nhis and Clinical Characteristics of the Study Cohort

CA = celiac artery, COPD = chronic obstructive pulmonary disease, D-An = dissecting aneurysms, F-An = fusiform aneurysms, No. = number, RA = renal artery, SA = segmental artery, S-An = saccular aneurysms, SMA = superior mesenteric artery.

Values are number (percentage), or mean \pm SD.

Others: one case with colon carcinoma and one with hemorrhagic stroke.

Technical Details

There was a gradual decrease in the mesh porosity when the number of stents increased: the mesh porosity was 85.2% for a single-layer stent, which dropped to 72.2% (IQR: 71.9-72.9%), 60.5% (IQR: 60.4-62.8%), and 52.4% (IQR: 51.0-54.1%) for 2, 3, and 4 overlapping stents, respectively. Previous studies have demonstrated that the mesh porosity of the bare metal stent is the main factor determining the local hemodynamic effect associated with subsequent thrombosis, and suggested that optimal flow modulation effect might achieve with an stent porosity of 50-70%.¹⁷⁻²⁰ Therefore, with 3 or more layers of bare stents overlapped, the overall mesh porosity would reach the effective level. In this study, 3.3 ± 1.0 bare stents were deployed for each patient on average.

Technical failure occurred in one patient due to the severe angulation of the diseased aortic segment, which prohibited the second stent from being advanced to the target location after the first one was deployed. More details about the procedure can be found in Table 1. In 19 patients whose sac pressure was monitored during the procedure, no significant pressure decrease was documented after stenting (mean adjusted sac systolic pressure from 141.2 ± 20.6 to 138.2 ± 17.4 mm Hg, P = 0.22) (please refer to Supplemental Digital, http:// links.lww.com/MD/A91 for more details).

Post-operative mortality caused by pulmonary infection was seen in an 87-year-old male. Three patients presented with access site hematoma, which resolved prior to discharging. No adverse event was observed in other patients. There was no significant change in hemoglobin (118.6 \pm 20.7 g/L pre-operatively compared with 116.1 \pm 17.9 g/L post-operatively, P = 0.09) and renal function $(106.4 \pm 39.4 \text{ mmol/L} \text{ vs} 110.5 \pm 46.1 \text{ mmol/L},$ P = 0.14).

Follow-Up Results

Pre-operative CTA showed a baseline level of mean STR of $18.1 \pm 14.9\%$ and an average aneurysm diameter of 53.4 ± 13.6 mm. The STR increased to $93.6 \pm 9.5\%$ (P < 0.001), while the diameter decreased to 48.8 ± 13.9 mm (P < 0.001) during an average follow-up period of 20.9 ± 9.0 months (Figure 3A and B). Decrease of aneurysm diameter by more than 5 mm was observed in 15 patients. Aneurysm stabilization was documented in 26 cases and no significant aneurysm expansion was observed.

A total of 76 major visceral branches and 244 minor SAs were found within the stenting zone. During follow-up, 97.4% major branches and 97.1% minor branches remained patent. Loss of one RA was seen in 2 patients, but there was no sign of renal insufficiency in either of them due to the compensation of the contralateral kidney. Occlusion of one SA was noted in 7 patients without SCI symptom (Figure 4A and B). Overall clinical success rate reached 95.2% (40/42) in this study. One patient died of respiratory failure at 19 months, resulting in an all-cause mortality rate of 4.8% (2 out of 42). No aneurysm-related mortality was observed during the follow-up period.

Kaplan-Meier analysis showed the estimated proportion of patients with sac residual perfusion was $82.9 \pm 5.9\%$,

 $58.5 \pm 7.7\%$, $43.3 \pm 7.8\%$, and $38.9 \pm 8.1\%$ at 3, 6, 12, and 18 months, respectively. The average time required for the complete sac thrombosis was 16.3 ± 1.8 months. Estimated overall survival rate at 19 post-operative months was $93.2 \pm 4.9\%$. Expected patient survival time after stents implantation was 42.8 ± 1.5 months (Figure 4C and D).

Subgroup Analysis

The aneurysm flow pattern is dominated by the lesion morphology. The treatment outcome of the flow-diverting strategy may therefore vary in aneurysms of different morphology. Based on the aneurysm shape, patients in this study were subdivided into saccular (S-An), fusiform (F-An), and dissecting (D-An) aneurysm groups. S-An seemed to respond the best to MOUS therapy. Significant aneurysm diameter decrease was only observed in S-An group (from 51.4 ± 13.3 to 43.5 ± 10.2 mm, P < 0.001; Figure 3A), while F-An and D-An tended to remain unchanged over time (59.4 ± 19.7 and 52.7 ± 9.3 mm pre-operatively vs 57.5 ± 21.0 and 51.5 ± 10.7 mm post-operatively, P = 0.06 and



FIGURE 3. Aneurysm diameter and sac thrombosis ratio change during follow-up. (A) Comparison of aneurysm diameter pre-surgery and during follow-up. (B) Comparison of pre- and post-operative sac thrombosis ratio in the whole study cohort, and in each subgroup. (C) Comparison of aneurysm diameter decrease ratio among the 3 types of aneurysms within the first follow-up year. (D) Comparison of the sac thrombosis ratio in the 3 subgroups at each follow-up point within the first year (S-An = saccular aneurysms, F-An = fusiform aneurysms, D-An = dissecting aneurysms, asterisk = statistically significant difference).



FIGURE 4. Kaplan–Meier analysis of the patency rate of side branches, the aneurysm thrombosis process, and the survival rate. (A) Patency rate of major side branches (celiac arteries, superior mesenteric arteries, and renal arteries) during follow-up. (B) Patency rate of minor segmental arteries over time. (C) Cumulative percentage of patients whose aneurysm sac was patent with residual perfusion during follow-up. (D) Estimated all-cause mortality rate of the cohort treated with multiple overlapping uncovered stents (MOUS).

0.07, respectively). The aneurysm diameter change ratio, defined as the ratio of the change in aneurysm maximum diameter during follow-up over the pre-operative value, was significantly higher in S-An group ($11.4 \pm 5.8\%$) at 12 months than in F-An and D-An groups $(4.9 \pm 4.0\% \text{ and } 2.5 \pm 4.3\%, P = 0.01 \text{ and } < 0.001, \text{ respect-}$ ively; Figure 3C). Although a significant increase in sac thrombus deposition was documented in all 3 groups after stenting (Figure 3B), the S-An group manifested fastest thrombosis in the first follow-up year (STR = $84.0 \pm 16.0\%$, $94.6 \pm 10.8\%$, and $97.9 \pm 6.6\%$ at 3, 6, and 12 months, respectively; Figure 3D), while the thrombus growth rate in dissecting aneurysms was the slowest (STR = $51.7 \pm 17.1\%$, $72.7 \pm 14.0\%$, and $82.1 \pm 11.8\%$ at each corresponding follow-up point. Ninety percent of saccular aneurysms (18/20) were totally thrombosed within 12 months, while the proportion was 37.5% (3/8) and 16.7% (2/12) in fusiform and dissecting aneurysms, respectively (P = 0.01 and<0.001, respectively).

DISCUSSION

Complicated aortic aneurysm involving vital side branches has been difficult to treat endovascularly. The advanced branched/fenestrated endografts have offered a feasible way of preserving major branches, but the procedure often requires customized devices and technical expertise in visceral branches' cannulation and stenting, which makes the encouraging figures from high-volume centers difficult to duplicate in less experienced ones. Moreover, such procedure could be technically challenging and time-consuming even for experienced surgeons, especially in the presence of unusual anatomy.²¹ Furthermore, current branched/fenestrated endografts are still not capable of preserving minor vital branches such as SAs, the revascularization of which during open surgical repair of thoracic aortic aneurysms has proven beneficial for spinal cord protection.²²

The emerging flow-diverting strategy may provide a new perspective on the side branches' maintenance while stabilizing

the aneurysm. By elevating the local resistance, the multilayer device effectively decreases the flow velocity and total blood volume flowing into the aneurysm, modulates local flow pattern, and eventually promotes thrombus formation.^{20,23} However, the deployment of bare metal stent cannot decrease the blood pressure in the sac, which is very different from the traditional graft stent. In this study, blood pressure in the sac was measured successfully in 19 patients, and results revealed that the local pressure did not change significantly after the stent deployment (from 141.2 ± 20.6 to 138.2 ± 17.4 mm Hg, P = 0.22). Nonetheless, same to the stent-grafts, those flowdiverting stents can also decrease the tensile stress of the aneurysm wall and reduce the risk of rupture. Its mechanism can be illustrated using the following first-order approximation: according to the Laplace law: $\sigma = (P \times r)/h$, average aneurysm wall tension (σ) is directly proportional to sac pressure (P) and lumen radius (r), while inversely proportional to aneurysm wall thickness (h). Traditional endografts provide a mechanical barrier between the aneurysm sac and normal blood flow, resulting in a reduced sac pressure and therefore leading to a decreased aneurysm wall tension; flow-diverters, on the other hand, promote the formation of mural thrombus that increases the effective wall thickness and decreases the lumen radius, and therefore reduces the aneurysm wall tension even though the sac pressure remains unchanged. However, it needs to be pointed out that as the sac thrombosis process and the subsequent protective efficacy might take months to reach an effective level, patients may remain exposed to the risk of aneurysm rupture for several months after stenting. With this consideration, those with an aneurysm judged to be approaching rupture should not be considered as candidates for this treatment strategy.

In this study, the aneurysm diameter decreased by 4.6 mm on average during the follow-up in the whole cohort. Contrast results have been reported including aneurysm expansion and rupture.^{4,7} Such events were however not observed in this study. It may be due to differences in patient enrollment, aneurysm morphology, and post-operative blood pressure control among the study population. Moreover, in this study we applied a layer-by-layer assembled MOUS strategy that permits flexible adjustment of the overall porosity by changing the number of stents until a significant decrease in sac flow velocity was achieved. Therefore, the risk of incomplete aneurysm exclusion could be minimized.

Subgroup analysis revealed that aneurysm morphology was related to the treatment outcome. Saccular aneurysms tended to thrombose faster after stenting compared with the other 2 groups, with 90% of them totally thrombosed at 12 months, leading to more significant aneurysm shrinkage. The slowest thrombosis process was observed in dissecting aneurysms, with 83.3% patients presenting with sac residual perfusion at 1-year follow-up. This result indicates that patients with saccular aneurysms might benefit the most from the flowdiverting strategy, and further follow-up is required to verify its treatment efficacy in fusiform and dissecting aneurysms.

A satisfactory performance of MOUS in side branches' preservation was documented. Overall branch patency rate reached 97.2% in the patient cohort. During follow-up, no symptomatic target organ ischemia was noted. Antiplatelet therapy with acetylsalicylic acid and clopidogrel has been suggested in the literature to maintain side branch patency,²⁴ but such therapy would undoubtedly impede the thrombosis process of the aneurysm sac.⁹ In this study, only patients with cardiac-cerebral vascular diseases were subjected to routine

anti-platelet therapy (15 patients), yet a satisfactory branch preservation rate was documented in all cases.

Despite the interesting findings in this study, some major limitations exist in the relatively small patient cohort and nonrandomized design. Besides, given the reports on aneurysm rupture despite thick mural thrombus, longer-term follow-up is required to demonstrate whether these currently stabilized aneurysms would evolve in the future, especially for fusiform and dissecting aneurysms. However, this pilot study could pave ways to future large-scale prospective clinical investigations and fundamental researches regarding the biological nature of the stent-induced thrombus.

In conclusion, the preliminary result from this pilot study indicates that with meticulous patient selection, flow-diverting strategy could be a feasible alternative to treat complicated aortic aneurysms involving vital branches, especially the saccular ones. Further prospective studies in a larger patient cohort are warranted to validate the potential of this technique in preserving side branches while stabilizing aneurysms.

ACKNOWLEDGMENTS

We are grateful to Dr Adam J Brown, University of Cambridge for his valuable suggestions in preparing the manuscript. Help from Daihan Zhou in statistical analysis is also appreciated.

REFERENCES

- Geremia G, Haklin M, Brennecke L. Embolization of experimentally created aneurysms with intravascular stent devices. *Am J Neuroradiol.* 1994;15:1223–1231.
- Wong GKC, Kwan MCL, Ng RYT, et al. Flow diverters for treatment of intracranial aneurysms: current status and ongoing clinical trials. *J Clin Neurosci.* 2011;18:737–740.
- Ruffino MA, Rabbia C. Endovascular repair of peripheral and visceral aneurysms with the cardiatis multilayer flow modulator: one-year results from the Italian Multicenter Registry. *J Endovasc Ther.* 2012;19:599–610.
- Lazaris A, Maheras A, Vasdekis S. A multilayer stent in the aorta may not seal the aneurysm, thereby leading to rupture. *J Vasc Surg.* 2012;56:829–831.
- Sultan S, Hynes N, Sultan M. When not to implant the multilayer flow modulator: lessons learned from application outside the indications for use in patients with thoracoabdominal pathologies. *J Endovasc Ther.* 2014;21:96–112.
- Debing E, Aerden D, Gallala S, et al. Stenting complex aorta aneurysms with the cardiatis multilayer flow modulator: first impressions. *Eur J Vasc Endovasc Surg.* 2014;47:604–608.
- Sultan S, Hynes N. One-year results of the multilayer flow modulator stent in the management of thoracoabdominal aortic aneurysms and type B dissections. *J Endovasc Ther.* 2013;20:366– 377.
- Ferrero E, Gibello L, Ferri M. Aortic arch rupture after multiple multilayer stent treatment of a thoracoabdominal aneurysm. *J Vasc Surg.* 201310.1016/j.jvs.2013.08.006.
- Zhang YX, Lu QS, Feng JX, et al. Endovascular management of pararenal aortic aneurysms with multiple overlapping uncovered stents. J Vasc Surg. 2013;58:616–624.
- Lu Q, Feng J, Zhou J, et al. Endovascular repair of ascending aortic dissection: a novel treatment option for patients judged unfit for direct surgical repair. J Am Coll Cardiol. 2013;61:1917–1924.

- Bley TA, Duffek CC, François CJ, et al. Presurgical localization of the artery of Adamkiewicz with time-resolved 3.0-T MR angiography. *Radiology*. 2010;255:873–881.
- Koshino T, Murakami G, Morishita K. Does the Adamkiewicz artery originate from the larger segmental arteries? *J Thorac Cardiovasc Surg.* 1999;117:898–905.
- Amabile P, Grisoli D, Giorgi R. Incidence and determinants of spinal cord ischaemia in stent-graft repair of the thoracic aorta. *Eur J Vasc Endovasc Surg.* 2008;35:455–461.
- Cooper D, Walsh S, Sadat U. Neurological complications after left subclavian artery coverage during thoracic endovascular aortic repair: a systematic review and meta-analysis. *J Vasc Surg.* 2009;49:1594–1601.
- Baril DT, Carroccio A, Ellozy SH, et al. Endovascular thoracic aortic repair and previous or concomitant abdominal aortic repair: is the increased risk of spinal cord ischemia real? *Ann Vasc Surg.* 2006;20:188–194.
- Chaikof EL, Blankensteijn JD, Harris PL, et al. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg. 2002;35:1048– 1060.
- Rhee K, Han MH, Cha SH. Changes of flow characteristics by stenting in aneurysm models: influence of aneurysm geometry and stent porosity. *Ann Biomed Eng.* 2002;30:894–904.

- Augsburger L, Farhat M, Reymond P, et al. Effect of flow diverter porosity on intraaneurysmal blood flow. *Klin Neuroradiol*. 2009;19:204– 214.
- Liou TM, Li YC. Effects of stent porosity on hemodynamics in a sidewall aneurysm model. J Biomech. 2008;41:1174–1183.
- Sfyroeras GS, Dalainas I, Giannakopoulos TG, et al. Flow-diverting stents for the treatment of arterial aneurysms. *J Vasc Surg.* 2012;56:839–846.
- Riga CV, Jenkins MP. Best surgical option for thoracoabdominal aneurysm repair—the hybrid approach. Ann Cardiothorac Surg. 2012;1:339–344.
- 22. Woo EY, Mcgarvey M, Jackson BM, et al. Spinal cord ischemia may be reduced via a novel technique of intercostal artery revascularization during open thoracoabdominal aneurysm repair. J Vasc Surg. 2007;46:421–426.
- Zhang Y, Lu Q, Jing Z. Multilayer stents, a new progress in the endovascular treatment of aneurysms. *Chin Med J.* 2013;126:536– 541.
- Euringer W, Südkamp M, Rylski B, et al. Endovascular treatment of multiple HIV-related aneurysms using multilayer stents. *Cardiovasc Interv Radiol.* 2012;35:945–949.