Is endovascular treatment with multilayer flow modulator stent insertion a safe alternative to open surgery for high-risk patients with thoracoabdominal aortic aneurysm?

Carolline Pinto, George Garas*, Leanne Harling, Ara Darzi, Roberto Casula, Thanos Athanasiou

Department of Surgery and Cancer, Imperial College London, St Mary's Hospital, London, United Kingdom

HIGHLIGHTS

- There is a paucity of evidence on the subject with complete absence of RCTs.
- The studies support MFMS as a safe alternative in the management of high-risk TAAA.
- MFMS maintains branch vessel patency when used in accordance to the IFU.
- MFMS should not be used outside the IFU as undesirable outcomes have been reported.
- A personalised approach is advised considering patient comorbidities and wishes.

ABSTRACT

A best evidence topic in cardiothoracic and vascular surgery was written according to a structured protocol. The question addressed was whether endovascular treatment with multilayer flow modulator stents (MFMS) can be considered a safe alternative to open surgery for high-risk patients with thoracoabdominal aortic aneurysm (TAAA). Altogether 27 papers were identified using the reported search, of which 11 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes, results, and study limitations are tabulated. The outcomes of interest were all-cause survival, aneurysm-related survival, branch vessel patency and major adverse events. Aneurysm-related survival exceeded 78% in almost all studies, with the exception of one where the MFMS was inserted outside the instructions for use. In that study the aneurysm-related survival was 28.9%. The branch vessel patency was higher than 95% in 10 studies and not reported in one. At 12-month follow-up, several studies showed a low incidence of major adverse events, including stroke, paraplegia and aneurysm rupture. We conclude that MFMS represent a suitable and safe treatment for high-risk patients with TAAA maintaining branch vessel patency when used within their instructions for use. However, a number of limitations must be considered when interpreting this evidence, particularly the complete lack of randomised controlled trials (RCTs), short follow-up in all studies, and heterogeneity of the pathologies among the different populations studied. Further innovative developments are needed to improve MFMS safety, expand their instructions for use, and enhance their efficacy.

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1. Introduction

A best evidence topic was constructed according to a structured protocol. This is fully described in a previous publication [1].

2. Clinical scenario

You have been referred an 85-year-old man with an asymptomatic thoracoabdominal aortic aneurysm (TAAA) type II (Crawford's classification) diagnosed on computed tomography angiogram with a maximum diameter of 68 mm in the descending aorta. Comorbidities include chronic obstructive pulmonary disease (COPD), obesity, diabetes mellitus type II, hypertension, and
chronic renal failure. The patient tells you that in view of his age and comorbidities he is keen for a minimally invasive approach and asks you whether endovascular treatment with insertion of multilayer flow modulator stents (MFMS), a new treatment which his family read about on Google, would be a suitable option for him. To confirm the therapeutic option and achieve the best possible outcome in this high-risk patient, you perform a literature review yourself.

3. Three-part question

In [high-risk patients with thoracoabdominal aortic aneurysm] are [multilayer flow modulator stents] a safe alternative to open surgery for achieving [better survival and lower morbidity]?

4. Search strategy

A literature search was performed using PubMed, Ovid, Embase, and Cochrane databases using the terms (“aortic aneurysm, thoracic”[MeSH Terms] OR (“aortic”[All Fields] AND “aneurysm”[All Fields] AND “thoracic”[All Fields]) OR “thoracic aortic aneurysm”[All Fields] OR (“thoracoabdominal”[All Fields] AND “aortic”[All Fields] AND “aneurysm”[All Fields]) OR “thoracoabdominal aortic aneurysm”[All Fields]) AND multilayer[All Fields] AND flow[All Fields] AND (“stents”[MeSH Terms] OR “stents”[All Fields] OR “stent”[All Fields]).

In addition, the reference lists of the relevant papers were searched. The search was current as of 23rd January 2017.

5. Search outcome

Twenty seven papers were identified using the reported search. Two authors (C.P. and G.G.) independently assessed the titles and abstracts of the identified articles to determine potential relevance. Any disagreement was resolved by discussion or with the opinion of the senior author (T.A.) After reviewing the abstracts, 21 papers were selected to be fully appraised in view of relevance and methods used. From these, 2 were short communications, 2 involved overlap of patient groups (the most recent was included), 6 were irrelevant, one was a narrative review, and one article was in French (all excluded except for the latter). Inclusion criteria included studies of any size, prospective or retrospective in design that assessed outcomes for patients with thoracoabdominal aneurysm. All patients included had to have received appropriate treatment. Exclusion criteria included studies reporting on patients with peripheral or visceral aneurysms. Narrative review articles and studies where the patients had not been subgrouped according to the anatomical site of the aneurysm to allow distilling of the evidence specifically for thoracoabdominal aneurysms were also excluded. Based on design, number of patients and origin (high volume/specialised centres and national registries) 11 papers were chosen as representative to answer the clinical question.

6. Results

The results of the 11 papers (one meta-analysis, 4 prospective studies, and 6 retrospective studies) are summarised in Table 1.

7. Discussion

In 2016, Hynes et al. [2] published a meta-analysis of MFMS reviewing data on 171 patients with complex aortic pathology (59.1% had TAAA). They found that the aneurysm-related survival rate was 78.7% at 1 year and 66.6% at 18 months. At 18 months, this rate was 93.3% within the instructions for use (IFU) subgroup in contrast to a rate of 25.6% for patients treated outside the IFU. Technical success was 76.6%, with 95.5% of technical failures occurring in cases performed outside the IFU. All-cause survival rate was 53.7% at 1 year and 37.4% at 18 months. There were no cases of spinal cord ischemia, renal insult or stroke.

Lowe et al. [3] analysed the outcomes of MFMS in 14 patients. Among these, 50% had TAAA. All-cause, aneurysm-related and growth-free survivals were 79%, 86% and 28.5% respectively at 1 year. The 30-day mortality was 7% whilst at a mean follow-up of 22.8 months it reached 50% with one rupture. There were MFMS dislocations in 28.6% of patients with 35% of cases requiring reintervention.

In their prospective study, Bouayed et al. [4] assessed the effects of use of MFMS in 41 aortic lesions. Among these, 20 were TAAA. 30-day mortality was 5.26% due to aneurysmal rupture and myocardial infarction whilst 12-month mortality was 23.68%. The aneurysmal sac was not supplied in 30% of TAAA cases and poorly supplied in 70%. Visceral patency was 100%.

Vaisic et al. [5] evaluated one-year outcomes following the use of MFMS in 23 patients with type II and III TAAA. At 12 months, all-cause mortality was 4%, complete sac thrombosis was achieved in 75% of patients and branch patency rate was 96.5%. Moreover, at 12 months there were reinterventions in 22% of patients and the aneurysm diameter increased in 10% whilst remained stable in 90%.

Sultan et al. [6] presented the results of 103 patients treated with MFMS under IFU. Among the cases, 72.8% had TAAA. At 1 year, aneurysm-related survival was 91.7% (no rupture occurred), all-cause survival was 86.8% and the covered branch patency was 95.3%. The incidence of stroke and paraplegia were 1.9% and 0.99% respectively at 12 months.

In another study, Sultan et al. [7] appraised the consequences of treatment with MFMS outside the IFU in 38 patients, among which 39.5% had TAAA. During the follow up (10.0 ± 6.9 months), all-cause mortality was 89.5%, of which 71.1% were aneurysm-related. At 18 months, overall survival, freedom from aneurysm-related death and rupture-free survival were 17.5%, 25.0% and 31.5% respectively. Visceral branch occlusions were observed in 21% of patients. There were no reported cases of stroke or paraplegia.

Sultan and Hynes [8] retrospectively reviewed 1-year results of 55 patients, of which 56.4% had TAAA, treated with MFMS. At 1 year, aneurysm-related survival was 93.7% (no rupture occurred), all-cause survival was 84.8%, intervention-free survival was 92.4%, and all side branches were patent. Complications included bleeding (7.3%), stroke (3.6%) and reintervention (7.3%).

Henry et al. [9] analysed the use of MFMS in 18 patients (55.5% of which had TAAA). Technical success was 100% and 30-day mortality was 0%. At 8 months, aneurysm-related and all-cause survivals were 100% and 83.3% respectively, with branch patency rate being 100%. In the TAAA group, the mean aneurysm diameter decreased at 6 months.

Pane et al. [10], Debing et al. [11], and Polyzorou et al. [12] all reported similar outcomes following treatment of TAAA with MFMS. They concluded that use of the medical device is feasible and seems to be a solution for the management of TAAA. The authors also inferred that MFMS can stabilise aneurysm diameter and ensure the patency of collateral vessels.

When looking collectively at the existing evidence, there are certain important points for consideration. First and foremost, there is a complete absence of randomised controlled trials (RCTs) on the subject. Secondly, there are no long-term follow-up studies. Thirdly, a significant amount of heterogeneity exists in terms of the variety concerning both the anatomy (location) and pathology (type) of aneurysms treated with MFMS. As a result, certain studies contradict others, especially when it comes to reporting mid-term results with some authors concluding that “the treatment of
| Author, date and country | Patient Group | Study type (level of evidence) | Outcomes | Key results | Comments |
|-------------------------|---------------|--------------------------------|----------|-------------|----------|
| Hynes et al. [2], Ireland | 171 patients (mean age 68.8 years) | Meta-analysis of observational non-comparative studies and case series (level 2b) | Primary endpoint | Mean follow-up was 9 months | MFMS technology is able to treat thoracoabdominal pathology safely |
|                         | TAAA - 59.1% (type I 7.6%; type II 14%; type III 16.4%; type IV 9.5%; unclassified 11.1%) Descending thoracic aortic aneurysm - 0.6% AAs - 22.2% Type B dissections - 11.7% Saccular aneurysms - 8.2% Arch aneurysms - 4.7% | | Aneurysm-related survival | Aneurysm-related survival was 78.7% at 1 year and 66.6% at 18 months (mean follow-up 9 months, mean aneurysm diameter 6.7 ± 1.6 cm) | Poor outcomes were explained by a lack of appreciation of the device’s limitations and its application outside the IFU |
|                         | Secondary endpoints | | | | Randomised clinical trials, registries and continued assessment are essential before the MFMS can be widely disseminated |
|                         | Technical success | | | | |
|                         | All-cause survival | | | | |
|                         | Neurologic complications | | | | |
|                         | Renal impairment | | | | |
|                         | Visceral ischemia | | | | |
|                         | Branch vessel patency | | | | |
|                         | Aneurysm expansion | | | | |
|                         | Mean follow-up of 22.8 months | | | | |
|                         | At 1 year: | Mean follow-up was 9 months | | | |
|                         | All-cause survival - 79% | | | | |
|                         | Aneurysm - related survival - 86% (one rupture, one perioperative death) | | | | |
|                         | Growth-free survival - 28.5% | | | | |
|                         | Visceral branch patency rate of 98% at 1 year (no embolic episodes or symptoms of ischemia) | | | | |
|                         | Median increase in aneurysm size of 9 mm at 12 months, and of 11 mm at mean follow up | | | | |
|                         | Branch patency rate of 97.8% | | | | |
|                         | 30-day mortality - 7% | | | | |
|                         | At mean follow-up 50% of patients died: Rupture - 7.1% Myocardial infarction - 14.3% (7.1% procedure-related and 7.1% unrelated at 17 months) COPD/pneumonia (not device or procedure-related) - 7.1% Multigorgan failure post implantation - 7.1% Unknown - 14.3% | | | | |
|                         | MFMS dislocation in 28.6% of patients | | | | |
|                         | Reinterventions in 35% of patients, with 7% of post-re-intervention death Mean follow-up was 12 months (1–20 months) “Initial technical success” was 100% with no cases of paraplegia, stroke, or mesenteric ischemia | | | | |
|                         | Conclusions | | | | |
| Lowe et al. [3], United Kingdom | Fourteen patients with mean age of 74.6 years | Prospective cohort study (level 2a) | Growth-free survival | At 1 year: All-cause survival - 79% Aneurysm - related survival - 86% (one rupture, one perioperative death) Growth-free survival - 28.5% Visceral branch patency rate of 98% at 1 year (no embolic episodes or symptoms of ischemia) Median increase in aneurysm size of 9 mm at 12 months, and of 11 mm at mean follow up Branch patency rate of 97.8% 30-day mortality - 7% At mean follow-up 50% of patients died: Rupture - 7.1% Myocardial infarction - 14.3% (7.1% procedure-related and 7.1% unrelated at 17 months) COPD/pneumonia (not device or procedure-related) - 7.1% Multigorgan failure post implantation - 7.1% Unknown - 14.3% MFMS dislocation in 28.6% of patients Reinterventions in 35% of patients, with 7% of post-re-intervention death Mean follow-up was 12 months (1–20 months) “Initial technical success” was 100% with no cases of paraplegia, stroke, or mesenteric ischemia | MFMS had little influence on the natural history of complex aortic aneurysms The device was unstable and dislocated frequently None of the aneurysms treated shrank and the majority of aneurysms in patients who survived over 12 months continued to grow The role of MFMS remains unclear Small number of patients Variety of pathologies |
|                         | Varieties of pathologies | | | | |
|                         | Conclusions | | | | |
| Bouayed et al. [4], Algeria | Thirty eight patients on which 41 procedures were performed on 41 lesion locations | Prospective cohort study (level 2a) | Aneurysm location | Conclusions | Multilayer stents may represent a treatment option for dissection and complex aortic aneurysms in frail patients which would (continued on next page) |
Table 1 (continued)

| Author, date and country | Patient Group | Study type (level of evidence) | Outcomes | Key results | Comments |
|--------------------------|---------------|--------------------------------|----------|-------------|----------|
|                           |               |                                | Month    |             |          |
|                           |               |                                | all-cause mortality | Mean length of hospital stay was 7 days (4–14 days) |          |
|                           |               |                                | Complications | Complications |          |
|                           |               |                                | Need for open conversion | Three complications relating to the surgical approach occurred, all treated surgically “with success” |          |
|                           |               |                                | Length of hospital stay | Two patients developed post-operative renal failure, one of them requiring haemodialysis (2.63%) |          |
|                           |               |                                |          | There was no need for open conversion |          |
|                           |               |                                |          | Mortality |          |
|                           |               |                                |          | 30-day mortality was 5.26% One patient died due to aneurysmal rupture in the first postoperative day and one died following a massive myocardial infarction after the procedure |          |
|                           |               |                                |          | 12-month mortality was 23.68% (9 deaths, none related to the aneurysm) |          |
|                           |               |                                |          | Limitations |          |
|                           |               |                                |          | Small number of patients |          |
|                           |               |                                |          | Heterogeneous groups (in terms of aneurysm type and location) |          |
|                           |               |                                |          | No controls |          |
|                           |               |                                |          | Single centre study |          |
| Vaislic et al. [5], France| Twenty-three high surgical risk patients with mean age of 75.8 years | Prospective multicentre non-randomised trial (level 2a) | Primary endpoints | Follow-up of 12 months |          |
|                           |               |                                |          | All-cause mortality |          |
|                           |               |                                |          | Complete sac thrombosis |          |
|                           |               |                                |          | Branch vessel patency |          |
|                           |               |                                |          | Secondary endpoints |          |
|                           |               |                                |          | Major adverse events |          |
|                           |               |                                |          | Reintervention |          |
|                           |               |                                |          | Technical endpoints |          |
|                           |               |                                |          | Technical success |          |
|                           |               |                                |          | Change in aneurysm sac size |          |
|                           |               |                                |          | Volume Analysis |          |
|                           |               |                                |          |                         | Conclusions |
|                           |               |                                |          |                         |          |
|                           |               |                                |          |                         | Successful endovascular treatment with MFMS |          |
|                           |               |                                |          |                         | Radiographic evidence of progressive sac thrombus formation |          |
|                           |               |                                |          |                         | No cases of spinal cord ischemia, aneurysm rupture, device migration and reported systemic complications |          |
|                           |               |                                |          |                         | Limitations |          |
|                           |               |                                |          |                         | Non-randomised trial |          |
|                           |               |                                |          |                         | 12 months of follow up (longer time expected for sac shrinkage in large TAAA involving visceral branches) |          |

Mean aneurysm diameter 6.5 ± 0.9 cm
Sultan S et al. [6], Ireland
One hundred and three patients with mean age of 69.2 years
Crawford TAAA - 72.8% of the presented pathologies:
Type I - 10.7%
Type II - 13.6%
Type III - 25.2%
Type IV - 23.3%
Arch aneurysms - 6.8%
AAA - 14.6%
Stanford type-B dissection - 5.8%
Mean aneurysm diameter 6.4 ± 1.66 cm
Crawford TAAA - 72.8% of the presented pathologies:
Type I - 10.7%
Type II - 13.6%
Type III - 25.2%
Type IV - 23.3%
Arch aneurysms - 6.8%
AAA - 14.6%
Stanford type-B dissection - 5.8%
Mean aneurysm diameter 6.4 ± 1.66 cm

Primary endpoints at 1 year
Rupture and aneurysm-related survival
All cause survival
Patency of visceral branches
Incidence of stroke and paraplegia

Technical endpoints
Aneurysm sac volume modulation at 1 year

Technical success
One-year freedom from reintervention

Mean follow-up was 11.6 ± 3.31 months
(median = 6 months)
At 1 year:
Aneurysm related survival - 91.7% (no rupture)
All-cause survival - 86.8%
Covered branch patency - 95.3%
Incidence of stroke - 1.9%
Incidence of paraplegia - 0.99%
Total volume increased - 6.79%
Thrombus volume increased - 21.3%
Maximum sac volume increased - 12.6%
Residual flow volume decreased - 11.78%
Total average increase in sac volume - 5.07%

Mean aneurysm diameter 6.4 ± 1.66 cm

Sultan et al. [7], Ireland
Thirty-eight patients with mean age of 71 years treated with MFMS outside the IFU
Crawford TAAA - 39.5% of the presented pathologies:
Type I - 2.6%
Type II - 18.4%
Type III - 13.2%
Type IV - 5.3%
66.7% of TAAA were ruptured at presentation
Mean aneurysm diameter 7.1 ± 1.1 cm
Crawford TAAA - 39.5% of the presented pathologies:
Type I - 2.6%
Type II - 18.4%
Type III - 13.2%
Type IV - 5.3%
66.7% of TAAA were ruptured at presentation
Mean aneurysm diameter 7.1 ± 1.1 cm

Primary endpoints
Rupture
Aneurysm-related death
All-cause mortality
Occlusion of visceral branches
Stroke
Paraplegia

Technical endpoints
Change in mean aneurysm diameter
Freedom from leaks
Technical success
Freedom from reintervention

Mean follow-up of 10.0 ± 6.9 months:
Aneurysm-related deaths - 71.1%
All-cause mortality - 89.5%
Freedom from aneurysm-related death was 37.5% at 12 months and 25% at 18 months
Rupture-free survival estimates were 39% at 12 months and 31.5% at 18 months
Overall survival was 29% at 12 months and 17.5% at 18 months
Visceral branch occlusions were observed in 21.0% of patients (pre-existing side branch stenosis >50% with calcification in all of the side branches that experienced postoperative complications)
No stroke and paraplegia
The average growth rate of aneurysm diameter was 0.12 ± 0.16 cm/month
Sac expansion occurred in all cases
No sac stabilization or shrinkage
Technical success was zero (in 81.6% of the cases there was a failure to land the device)
Reinterventions were required in 28.9% of patients for endoleak (failure modes I and II) or stent foreshortening
Factors with significance influence on the risk of aneurysm-related death: maximum aneurysm diameter (p = 0.025), previous TEVAR (p = 0.03) and inadequate overlap between MFMS devices (p < 0.002)

Conclusions
Increasing sac volume, thrombus or diameter size was not associated with rupture
MFMS implantation instigates a process of aortic remodelling involving initial thrombus deposition, which slows between 6 and 12 months
MFMS is associated with less operative trauma, shorter procedure time and reduced hospital stay
The study has demonstrated the proof of concept of this disruptive technology
Limitations
Brevity of follow-up study
Variation in the pathologies and anatomies of patients
Conclusions
MFMS is a safe technique, at least in the short term (no perioperative complications), which reflects its simplicity of use
The MFMS is not a solution for patients living on borrowed time and should not be used indiscriminately in patients in whom other modalities of aortic repair are not feasible
The use of MFMS must adhere to the IFU
This technology commands further innovative developments and robust scientific and clinical data

(continued on next page)
| Author, date and country | Patient Group | Study type (level of evidence) | Outcomes | Key results | Comments |
|-------------------------|---------------|--------------------------------|----------|-------------|----------|
| Sultan et al. [8],      | Fifty-five patients with mean age of 64.3 years | Retrospective multicentre cohort study (level 2b) | Primary endpoint | Mean follow-up was 8.2 ± 5.3 months (median 6, range 3–18) | Conclusions |
| Ireland                 | Crawford TAAA - 56.4% of the presented pathologies: Type I - 14.3% Type II - 5.3% Type III - 16.4% Type IV - 20% | | Aneurysm related survival and rupture at 1 year | Aneurysm related survival at 1 year - 93.7% (no rupture occurred) All cause survival at 1 year - 84.8% Intervention free survival at 1 year - 92.4% | |
|                         | Mean aneurysm diameter 6.04 ± 1.66 cm | | Secondary endpoints | Covered branch patency rate of 100% at 1 year | |
|                         | Mean follow-up was 8.2 ± 5.3 months (median 6, range 3–18) | | All-cause survival | Adverse Events at 1 year Bleeding - 7.3% Stroke - 3.6% | Increase sac size did not lead to rupture |
|                         | | | Reintervention | Reintervention at 1 year - 7.3% | The MFMS offers promise for resolution of complex thoracoabdominal pathology with off-the-shelf availability |
| Henry et al. [9],      | Eighteen high surgical risk patients (mean age 67 years) | Retrospective case series (level 3) | Technical endpoints | Technical success of 98.2% | Further development and technical refinement is required |
| France                  | Crawford TAAA - 55.5% (mean age 56 year-old) Type I - 22.2% Type II - 11.1% Type IV - 22.2% | | Technical success | 30-day mortality Technical success of 100% | Long-term follow-up of the registry patients is mandatory before establishing a randomised controlled study |
|                         | Aneurysm diameter - 60 –130 mm | | Rates of change in total sac, thrombus and flow volumes | The ratio of thrombus to total volume stayed almost constant over the 12 months at 0.48 (p = 0.743) The ratio of flow to total volume fell from 0.21 to 0.12 at 12 months (p = 0.069) | |
| Pane et al. [10], Italy | Eight patients with mean age of 75.5 years | Retrospective case series (level 3) | Technical success | Mean follow-up of 8 months | Conclusions |
|                         | Aortic Aneurysms - 50% TAAA type II - 25% TAAA type IV - 12.5% JAAA - 12.5% | | Mortality | Technical success of 87.5% | MFMS can help prevent aneurysm-related mortalities while maintaining branch vessel patency |
|                         | Mean follow-up was 22.1 months | | 30-day mortality | Technical success of 100% | Treatment with MFMS leads to progressive aneurysm sac thrombosis and shrinkage |
|                         | | | At mean follow-up: | Aneurysm- related survival of 100% All-cause survival of 83.3% Intervention-free survival of 100% Branch patency rate of 100% | Additional study and follow up needed |
|                         | | | Aneurysm | TAAA group Mean diameter reduction at 6 months (17.25 mm reduction for transverse diameter (p = 0.009) and 13.83 mm for the anteroposterior diameter (p = 0.011)) Mean follow-up was 22.1 months | Limitations |
|                         | Mean follow-up was 22.1 months | | Aneurysm diameter | Mean diameter reduction at 6 months (17.25 mm reduction for transverse diameter (p = 0.009) and 13.83 mm for the anteroposterior diameter (p = 0.011)) | Small number of patients |
|                         | | | All-cause survival | All-cause survival of 100% | |
|                         | | | All-cause survival | All-cause survival of 100% | |
|                         | | | All-cause survival | All-cause survival of 100% | |
|                         | | | All-cause survival | All-cause survival of 100% | |

Limitations

- Brevity of follow-up study
- Variation in the pathologies and anatomies of the patients treated
- Issues of registry: data collection, patient compliance and the variety of follow-up protocols and pharmacotherapies

Conclusions

- MFMS implantation instigates a process of aortic remodelling involving initial thrombus deposition
- The MFMS offers promise for resolution of complex thoracoabdominal pathology with off-the-shelf availability
- Further development and technical refinement is required
- Long-term follow-up of the registry patients is mandatory before establishing a randomised controlled study
- MFMS can help prevent aneurysm-related mortalities while maintaining branch vessel patency
- Treatment with MFMS leads to progressive aneurysm sac thrombosis and shrinkage
- Additional study and follow up needed
- Small number of patients

MFMS may represent a viable alternative to the endovascular approach in treating aortic conditions

MFMS can stabilize aneurysm diameter and ensure the patency of collateral vessels

Limitations
| Mean max aneurysm diameter | complications | MFMS and branch patency rate of 100% during follow up | Small series - results must be confirmed by larger series and longer follow-up studies |
|---------------------------|---------------|-----------------------------------------------------|----------------------------------------------------------------------------------|
| 6.9 cm                    | Patency of collateral vessels | No secondary endovascular or open surgical procedures |                                                                                  |
|                           | Volume analysis | In aortic aneurysms, the total aneurysm volume increased 7.6% at 12 months |                                                                                  |
|                           |                | Overall trend to increase in thrombosis was observed in all cases |                                                                                  |

Debing et al. [11], Belgium

| Six patients with mean age of 74 years | Technical success | Median follow-up was 10 months | Conclusions |
|----------------------------------------|-------------------|-------------------------------|-------------|
| Prospective case series (level 3)      | Technical success | 30-day mortality | Technical success of 100% |
|                                        | Aneurysm-related survival | 30-day mortality | 16.7% |
|                                        | All-cause survival | Aneurysm-related survival | 83.3% (16.7% of patients died due to aneurysm rupture) |
|                                        | Side branch patency | Branch patency rate | 100% |
|                                        | Volume analysis | 66.7% of aneurysms were completely thrombosed between 1 and 6 months after the procedure | |
|                                        | Reintervention | At 6 months, the sac volume was decreased in 33.3% of patients, increased in 33.3% patients and remains stable in 16.7% | |
|                                        |                   | No stent migrations, retractions, thrombosis, fractures, or reinterventions | |
|                                        |                   | Mean follow-up for the thoracic aneurysm was 28 months, for the aortic aneurysms was 12 months and for thoracoabdominal aneurysm 12 months | |
|                                        |                   | Technical success of 100% | |
|                                        |                   | 30-day mortality | 9.1% |
|                                        |                   | All-cause survival | Aneurysm-related survival and all-cause survival | 90.9% |
|                                        |                   | Side branch patency | The 6 and 12 month follow up CT angiograms showed patent arterial side branches, thrombus inside the sac or shrinkage of the sac |
|                                        |                   | Adverse Events | Adverse events Stroke | 4.5% |
|                                        |                   |                 | Myocardial Infarction | 4.5% |
|                                        |                   |                 | No vascular or systematic complications | |

Polydorou et al. [12], Greece

| Twenty-two high risk patients with mean age of 67 years | Technical success | Median follow-up was 10 months | Conclusions |
|---------------------------------------------------------|-------------------|-------------------------------|-------------|
| Retrospective case series (level 3)                     | Technical success | 30-day mortality | Technical success of 100% |
|                                                        | Aneurysm-related survival | 30-day mortality | 9.1% |
|                                                        | All-cause survival | Aneurysm-related survival and all-cause survival | 90.9% |
|                                                        | Side branch patency | The 6 and 12 month follow up CT angiograms showed patent arterial side branches, thrombus inside the sac or shrinkage of the sac |
|                                                        | Adverse Events | Adverse events Stroke | 4.5% |
|                                                        |                   | Myocardial Infarction | 4.5% |
|                                                        |                   | No vascular or systematic complications | |

Abbreviations: MFMS — multilayer flow modulator stent; TAAA — thoracoabdominal aortic aneurysm; TAA — thoracic aortic aneurysm; AAA — abdominal aortic aneurysm; JAAA — juxtarenal abdominal aortic aneurysm; IFU — indications for use; TEVAR — thoracic endovascular aortic repair; COPD — chronic obstructive pulmonary disease; SMA — superior mesenteric artery.
aneurysms with MFMS seems to have encouraging mid-term results" [10] whilst others reporting that “the role of MFMS remains unclear” [3]. Despite the many limitations in the literature, there seems to be a consensus that MFMS, when used within their IFU, may represent a valuable option in those patients where open surgery is deemed high-risk. Finally, existing studies also concur that in addition to robust scientific and clinical data, further innovative developments are needed to improve MFMS safety, expand their instructions for use, and enhance their efficacy.

8. Clinical bottom line

In addition to the mortality associated with open TAAA repair, fundamental risks include compromising the blood flow to the spinal cord and/or viscera. In this context, MFMS appear to represent a safe alternative in the management of complex aneurysms. In this paper, the outcomes in patients with TAAA undergoing endovascular repair with MFMS were evaluated. Several studies showed that the use of MFMS in the treatment of TAAA is associated with a low incidence of complications, including stroke, paraplegia and aneurysm rupture. In addition, these studies demonstrated acceptable rates of aneurysm-related survival and visceral branch patency. On the other hand, undesirable outcomes have been reported when the MFMS is used outside the IFU.

Thus, we conclude that endovascular treatment with MFMS insertion is a safe treatment for TAAA in high-risk patients, associated with maintenance of branch vessel patency, provided they are used in accordance to the IFU. However, a number of limitations must be considered when interpreting this evidence. Firstly, the complete lack of RCTs, secondly, the absence of long-term follow-up studies, and thirdly, the heterogeneity of the pathologies among the different populations studied. Despite these limitations, MFMS appear to offer a suitable and safe alternative to open surgery for TAAA cases where open surgery is deemed high-risk.

Ethical approval

Not required.

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Author contribution

C Pinto — conducted literature search and co-wrote article with G Garas.
G Garas — conducted literature search and co-wrote article with C Pinto.
L Harling — assisted in writing of article.
A Darzi — assisted in writing of article.

R Casula — conceived paper with T Athanasiou and assisted in writing of article.
T Athanasiou — conceived paper with R Casula and assisted in writing of article.

Conflicts of interest

None.

Trial registry number — ISRCTN

Not applicable.

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Not applicable.

Guarantor

George Garas.

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