Aggressive Surveillance is Needed to Detect Endoleaks and Junctional Separation Between Device Components after Zenith Fenestrated Aortic Reconstruction

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Abstract

Objective:

Junctional separation and resulting type IIIa endoleak is a well-known problem after EVAR (endovascular aneurysm repair). This complication results in sac pressurization, enlargement, and eventual rupture. In this manuscript, we review the incidence of this late finding in our experience with the Cook Zenith Fenestrated endoprosthesis (ZFEN, Bloomington, IN)

Methods:

A retrospective review was performed of a prospectively maintained institutional ZFEN FEVAR (fenestrated EVAR) database capturing all ZFENs implanted at a large-volume, academic hospital system. Patients who experienced junctional separation between the fenestrated main body and distal bifurcated graft (with or without type IIIa endoleak) at any time after initial endoprosthesis implantation were subject to further evaluation of imaging and medical records to abstract clinical courses.

Results:

In 110 ZFENs implanted from October 2012 to December 2017 followed for a mean of 1.5 years, we observed a 4.5% and 2.7% incidence of clinically significant junctional separation and type IIIa endoleak, respectively. Junctional separation was directly related to concurrent type Ib endoleak in all five patients. Three patients presented with sac enlargement. One patient did not demonstrate any evidence of clinically significant endoleak and had a decreasing sac size during follow-up imaging. The mean time to diagnosis of modular separation in these patients was 40 months. Junctional separation was captured in surveillance in two patients and reintervened upon before manifestation of endoleak. However, the remaining three patients completed modular separation resulting in rupture and emergent intervention in two and an aortic-related mortality in the other.

Conclusions:

Junctional separation between the fenestrated main and distal bifurcated body with the potential for type IIIa endoleak is an established complication associated with the ZFEN platform. Therefore, we advocate for maximizing aortic overlap during the index procedure followed by aggressive surveillance and treatment of stent overlap loss captured on imaging.

Background

The Zenith Fenestrated aortic endoprosthesis was approved by the FDA in 2012 for short-neck infrarenal and juxtarenal aneurysms after successful demonstration of feasibility, safety, and effectiveness.[1] This modular device is custom-created with main body fenestrations to allow for the stenting of one or more visceral vessels in close proximity to the aneurysmal neck, effectively extending the proximal seal zone. As a result, the availability of this device outside of the purview of clinical trial regulations has generated a significant increase in ZFENs implanted outside manufacturer's IFU (instructions for use).[2] We have previously reported acceptable mid-term institutional results after our first one hundred implanted ZFENs.[3] Not surprisingly, the implantation of this complex aortic stent graft, often for challenging anatomy relative to open and conventional endovascular repair, has been associated with a higher rate of late complications and reinterventions.[4] One such feared complication after ZFEN is distal migration of the bifurcated graft resulting in component separation, sac pressurization, and catastrophic rupture. In this secondary investigation, we report our incidence and experience with this specific complication after ZFEN.

Methods

This study was approved by the Indiana University Institutional Review Board (#1311843883); informed consent was not required for the proposed protocol. A retrospective review, consistent with the principles outlined in the latest iteration of the Declaration of Helsinki, of a prospectively maintained ZFEN database was performed to isolate all junctional separation events diagnosed in patients treated with FEVAR from 2012 to 2017.[5] Suspected type III endoleaks arising because of fabric tears or via the junction of the visceral covered stents and the main body fenestrations were excluded leaving only component separations of the proximal and distal aortic pieces.

The preoperative and intraoperative decision making for ZFEN implantation at our institution has been described in detail elsewhere.[6] Among the IFU for the ZFEN device includes a minimal proximal neck length of 4 mm, proximal neck diameter of 19 – 31 mm, and proximal neck angulation of <45°. Maximum overlap is encouraged whenever possible between the aortic components with a minimum overlap of 2 stent increments or 36 mm (**Figure 1**). Postoperative surveillance after ZFEN at our institution consists of a serum creatinine and CT angiography (CTA) at one-month, six-months, and 12-months followed by annual scans thereafter. If evidence of endoleak or sac expansion were noted, intervals between scans were shortened at the discretion of the attending vascular surgeon. For patients with renal insufficiency, we performed surveillance imaging at the same intervals with the substitution of a noncontrasted CT and a mesenteric/renal/aortic duplex sonogram for the CTA.

Three-dimensional aortic reconstruction for all postoperative scans were performed in Aquarius Workstation (TeraRecon, Foster City, CA). Centerline measurements were obtained to generate junctional overlap changes over time for each individual. For measurement purposes, junctional overlap was defined as the distance from the distal, metallic edge of the proximal main body to the proximal, metallic edge of the distal bifurcated graft.

Results

From October 2012 to December of 2017, a total of 110 Zenith Fenestrated aortic stent grafts were implanted for short-neck infrarenal and juxtarenal aneurysms at our institution. The mean follow-up for this cohort was 1.5 ± 1.5 years. We observed five cases of component separation which were intervened upon at a mean time of 40 months after the index endoprosthesis implantation (**Table 1**).

Patient One

A 63M with a 64 mm juxtarenal AAA was repaired in April 2013 using a 32 x 124 mm proximal main body with bilateral renal artery fenestrations and a SMA (superior mesenteric artery) scallop. The distal bifurcated graft was in a 20 x 45 x 76 mm configuration. No endoleaks were noted at the first postoperative visit and junctional overlap at that time was 55 mm. Aortic anatomy remained stable until 18-months postprocedure, when a noncontrasted CT demonstrated residual sac enlargement to 69 mm. However, an aortic duplex did not show any evidence of endoleak. Two years after the index operation, repeat CTA was concerning for continued sac expansion to 74 mm with a decrease in modular overlap to 50 mm. An aortic duplex was repeated which did not demonstrate any flow to the residual sac. After discussion of more aggressive diagnostic options with the patient, he opted to continue noninvasive imaging and defer a diagnostic angiogram. At his 3-year postoperative visit, his residual sac was stable without endoleak evidence. Unfortunately, continued decrease in junctional overlap to 37 mm secondary to progressive angulation of the distal sac was unrecognized. The decision at that point was to continue follow-up surveillance without intervention.

Forty-five months after the index repair, the patient presented to an outlying hospital with sudden, severe abdominal pain in the setting of profound hypotension. A CTA demonstrated increased sac size to 93 mm with evidence of retroperitoneal hematoma and acute rupture (**Figure 2**). It was apparent that the right iliac limb had retracted secondary to continued distal aneurysmal degeneration, creating a large type Ib endoleak resulting in sac pressurization and progressive migration of the distal bifurcated graft. The patient quickly became unresponsive despite initiation of massive transfusion protocols. Eventually, the family decided to initiate comfort measures and withdraw heroic measures.

Patient Two

A 78M presented to us with a 70 mm juxtarenal AAA was repaired with a 34 x 107 mm ZFEN main body with bilateral renal artery small fenestrations and a large fenestration for the SMA in December 2013. The distal bifurcated graft was in a 24 x 62 x 76 mm configuration with the iliacs sealed

via 20 mm limb extensions. At his initial postoperative visit, a type II lumbar artery endoleak was visible with an initial junctional overlap of 50 mm. Twelve months after his index operation, follow-up CTA, once again, demonstrated the continued presence of the type II endoleak, sac expansion to 76 mm, and a decrease in junctional overlap to 38 mm. As a result, we performed an angiogram where it was noted that the residual sac was being fed from an iliolumbar branch off the hypogastric artery; an adequate angiographic result was noted after targeted coil embolization of this hypertrophied collateral.

At his 24-month follow-up, a CTA demonstrated continued sac expansion to 80 mm without a clear source of endoleak; junctional overlap was now 30 mm. At this point, we suspected a type Ib endoleak was continuing to pressurize the sac. Therefore, we took the patient to the operating theatre where a provoked angiogram confirmed the suspected Ib endoleak. We extended the distal graft with a Cook 11 x 107 mm iliac limb after embolization of the hypogastric artery. Additionally, we placed a 40 x 100 mm Palmaz stent at the modular junction and reinforced it with Aptus endoanchors (Medtronic, Minneapolis, MN).

Unfortunately, 34-months postprocedure, surveillance CTA once again was concerning for sac enlargement to 90 mm in the setting of large type II endoleak. Angiogram demonstrated another hypertrophied iliolumbar vessel off the previously intervened side pressuring the residual sac. Therefore, translumbar coil embolization was successfully performed (**Figure 3**). We are currently continuing close follow-up on this patient to determine the effects of our latest reintervention.

Patient Three

A 77M with an 80 mm juxtarenal AAA was treated in December 2014 with a 36 x 122 mm ZFEN proximal body containing bilateral renal artery small fenestrations and a SMA scallop. The distal bifurcated graft was in a 12 x 28 x 76 mm configuration and sealed distally with bilateral 24 mm iliac limb extensions. The first postoperative CTA did not demonstrate any evidence of endoleak with an established junctional overlap of 40 mm. One year later, the patient presented to an OSH with new onset abdominal pain. CTA demonstrated an enlarging sac secondary to a new type Ib endoleak which was quickly repaired using 26 mm and 28 mm x 39 mm Cook aortic cuffs. Unfortunately, repeat imaging 20 months after the index repair again demonstrated increased sac size in the presence of a large lumbar type II endoleak which had not affected the junctional structure. The patient was taken to the OR for a successful transcaval embolization. Unfortunately, he failed to present for follow-up after this procedure.

In October 2017, 34 months after his index ZFEN, the patient, once again, presented to an OSH with abdominal pain. Repeat CTA demonstrated complete junctional separation and a type IIIa endoleak associated with aneurysm rupture. It appeared as if a recurrence of the type Ib endoleak caused distal migration of the bifurcated graft. The patient was immediately taken to the operative theatre where a 28 mm Gore (Flagstaff, AZ) aortic cuff was placed across the junction between proximal fenestrated and distal bifurcated bodies. The hypogastric was embolized and a Gore 16 x 100 mm iliac limb was deployed to fix the type Ib endoleak. The patient was eventually discharged to subacute rehabilitation where he recently completed a three-month rehabilitation stint.

Patient Four

A 69M with a 70 mm juxtarenal AAA was repaired in July 2015 with bilateral renal fenestrations in a 32 x 107 mm ZFEN proximal body. The distal bifurcated graft was created in a 12 x 28 x 76 mm configuration with a 24 x 74 mm left iliac limb and a right iliac extension using a 11 x 107 mm limb. His one-month postoperative visit was unremarkable without any evidence of endoleak. The initial junctional overlap was 35 mm. During this time period, he was diagnosed with lymphoma and began oncologic treatment. At eight-months postprocedure, a surveillance CTA performed for the oncologic team continued to lack evidence of endoleak in the setting of a stable residual sac; however, the junctional overlap had decreased to 26 mm secondary to increased distal angulation. The decision at this point was to hold intervention and observe how stent morphology changed at the next clinical visit.

In March of 2017, routine surveillance imaging for his lymphoma was concerning for a new type Ib endoleak without evidence of sac expansion. Additionally, a significant loss of junctional overlap to 14 mm was discovered upon closer inspection. Therefore, he was taken to the operating room for a hypogastric embolization, Cook iliac limb extension (11 x 107 mm), and placement of a Cook thoracic aortic cuff (28 x 80 mm) to bridge the modular aortic junction. Imaging in November of 2017 demonstrated both stable residual sac and aortic graft integrity without evidence of endoleak.

Patient Five

A 65M with schizophrenia presented with an 80 mm juxtarenal AAA. He was treated using a 28 x 124 mm proximal main body with bilateral renal artery small fenestrations and a SMA scallop in February 2013. A 12 x 28 x 121 mm distal bifurcated graft was implanted and extended with 24 x 74 mm iliac limb on the right a 12 x 122 mm on the left after successful preoperative left hypogastric embolization two weeks previously. Modular overlap after the initial procedure was 55 mm. Six months later, he developed a type Ib endoleak and a decrease in junctional overlap to 50 mm which was fixed

with a Cook iliac limb extension (13 x 107 mm). The aneurysm size continued to remain stable while junctional overlap decreased to 46 mm in December 2014. He was lost to follow-up after February of 2016, where it was noted that his aneurysm size remained stable in the setting of continued junctional overlap decrease to 37 mm.

After failing to present to multiple follow-up appointments, the patient presented to an OSH with new abdominal pain and hypotension in January 2018. A CTA at that time was concerning for a complete loss of junctional overlap in the setting of increasing distal aortic angulation (**Figure 4**). His infrarenal aortic segment was emergently relined using a Cook thoracic graft (28 x 109 mm). Fortunately, the patient ultimately survived to be discharged home.

Discussion

Using the ZFEN system, up to three modifications (no more than two of the same) in the main body consisting of a combination of fenestrations and scallops can be created to fit the visceral anatomy of the target patient.[4] In the U.S., all main bodies, regardless of proximal diameter, tapers distally to 24 mm where the overlap with the bifurcated piece occurs. Similarly, the only available size for the proximal diameter of the distal bifurcated piece is in a 24 mm configuration. As such, the only way to minimize the risk of separation is to maximize stent overlap in any given anatomy. This limitation was artificially created secondary to the guidelines imposed by the FDA after initial ZFEN approval as the clinical trials uniformly used this conformation. In contrast, European use of the ZFEN device is not subject to such strict regulations, and a smaller distal diameter (22 mm) of the proximal main body allows for a "friction fit" via distal upsizing with the 24 mm bifurcated piece.

With the introduction of modular EVAR, separation events were quickly recognized as a feared late complication which often results in rupture. For example, Skibba *et al* reviewed their experience with over 700 Endologix Powerlink (Irvine, CA) grafts implanted from 2006 to 2015. They observed a 2.4% long-term incidence of type IIIa endoleak which is comparable to other smaller reports over various EVAR platforms.[7,8] However, the incidence of those experiencing modular migration without endoleak remained unclear.[9] Additionally, the true incidence of clinically significant type IIIa endoleaks may be much higher. In 2016, our group published a 7.2% modular separation event rate associated with implantation of the AFX aortic graft which led to the voluntary withdrawal of a portion of available grafts by Endologix.[10] Interestingly, the FDA recently distributed a warning letter to interventionalists concerning the risk of type III endoleaks after EVAR while reinforcing the need for lifelong, aggressive surveillance after the index intervention.[11]

With progressive separation, junctional leaking causes pressurization of the aneurysmal sac, alters aortic morphology, and increases the risk for rupture. Additionally, increasingly turbulent flow dynamics exposures the patient to the risk of aortic thrombosis and acute limb ischemia.[10] It is possible that the risk of junctional separation may be increased in FEVAR compared to EVAR because of the inherent fixation of the fenestrated main body to the juxtarenal aorta allowing for only the migration of the distal pieces as sac morphology changes. Therefore, endoleaks which may have resulted in sac expansion, proximal stent migration, and type Ia endoleak in a patient with EVAR now presents with migration of the most proximal, unfixed stent. It is important to emphasize that all patients in this series had an endoleak which preceded their separation events. Two of these patients demonstrated isolated type II endoleaks which

resulted in eventual development of type Ib endoleaks. Therefore, the cavalier attitude towards "clinically insignificant" endoleaks should be abandoned with respect to ZFEN as postoperative endoleak rate are increased compared to EVAR. In our previously reported institutional experience, we found a 15% rate of identifiable endoleak by the last available CTA and a 31% incidence of endoleak at any point after graft implantation. Of these patients, 11 of 100 underwent reintervention for persistent endoleak.[3]

The problem with ZFEN migration has been examined before in a European case series. England *et al* performed a retrospective review of over 150 patients treated in the United Kingdom with a ZFEN device from 2003 and 2010. The authors reported a proximal main body migration incidence of 21% with a probability of being free from main body migration of 82%, 77%, and 77% at 12, 24, and 36 months, respectively. However, these migrations were generally clinically insignificant. Similarly, they noted a 13% iliac limb migration and a probability of being free from iliac limb migration at 85%, 82%, and 65% at 12, 24, and 36 months, respectively. The authors also reported a rate of component separation, as defined as a >4 mm migration between the main body and bifurcated graft, of 11.8%.[12] Unfortunately, it was unclear what proportion of the component migration events were clinically significant.

In this manuscript, we report five cases of clinically significant component separation between the ZFEN main body and the bifurcated distal graft over the first 110 patients treated. Three experienced ruptures while the remaining patients were appropriately reintervened on before a catastrophic event occurred. All were treated outside the ZFEN IFU. Four of these patients required a 24 mm iliac limb, the maximum available size, at their index operations while the remaining patient received a 20 mm limb. Previously, Schanzer *et al* reported that presence of endoleak, age ≥80 years, aortic neck diameter ≥28 mm, aortic neck angle ≥60°, and common iliac artery diameter ≥20 mm all independently predicted sac expansion after EVAR.[13] Certainly, our patients in this series all carry more than one of these predictors.

We observed a failure of the iliac limb seal zone which resulted in persistent type Ib endoleaks in all five patients. Large iliac diameters and type Ib endoleak should be taken in context of large residual sacs where lateral vector forces on components can increase distraction forces and thereby be at higher risk for type IIIa endoleak; Lemmon *et al* reported an OR >10 for this event to occur in the setting of a AAA >6.5 cm.[10] When these initial ZFEN cases were performed, no options of iliac branch endoprosthesis were available for challenging iliac anatomy. However, we have deployed, in several cases, iliac branch devices in combination with ZFEN to preserve at least one hypogastric artery and minimize the risk of distal leaks from aneurysmal iliac arteries. Additionally, we are also moving back towards plain anterior-posterior and lateral abdominal X-rays before clinic visits to optimally quantify

junctional overlap, a practice we employed with first-generation EVAR devices but lost favor as more reliable aortic platforms were introduced.

Our series has several limitations. The small population size makes generalization of this relatively rare complication more difficult. Additionally, we are missing follow-up imaging studies on several patients that were lost to follow-up or decided to establish care with other vascular surgeons closer to their homes. Therefore, it is more than probable that several graft migration events or complications were not captured by our medical system and records.

Conclusion

While the Zenith Fenestrated system has allowed clinicians to treat a wider range of aneurysmal pathologies, the need for careful surveillance with a high index of suspicion for junctional separation needs to be emphasized to prevent catastrophic rupture events.

References

1. Greenberg RK, Sternbergh WC, 3rd, Makaroun M, Ohki T, Chuter T, Bharadwaj P, et al. Intermediate results of a United States multicenter trial of fenestrated endograft repair for juxtarenal abdominal aortic aneurysms. *Journal of vascular surgery.* 2009;50(4):730-737.e731.
2. Vemuri C, Oderich GS, Lee JT, Farber MA, Fajardo A, Woo EY, et al. Postapproval outcomes of juxtarenal aortic aneurysms treated with the Zenith fenestrated endovascular graft. *J Vasc Surg.* 2014(1097-6809 (Electronic)).
3. Wang SK, Gutwein AR, Gupta AK, Lemmon GW, Sawchuk AP, Motaganahalli RL, et al. Institutional experience with the Zenith Fenestrated aortic stent graft. *Journal of vascular surgery.* 2018.
4. Oderich GS, Greenberg RK, Farber M, Lyden S, Sanchez L, Fairman R, et al. Results of the United States multicenter prospective study evaluating the Zenith fenestrated endovascular graft for treatment of juxtarenal abdominal aortic aneurysms. *J Vasc Surg.* 2014(1097-6809 (Electronic)).
5. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *Jama.* 2013;310(20):2191-2194.
6. Wang SK, Gutwein AR, Gupta AK, Lemmon GW, Sawchuk AP, Motaganahalli RL, et al. Institutional Experience with the Zenith Fenestrated Aortic Stent Graft. *Journal of vascular surgery.* 2017.
7. Keith CJ, Jr., Passman MA, Gaffud MJ, Novak Z, Pearce BJ, Matthews TC, et al. Comparison of outcomes following endovascular repair of abdominal aortic aneurysms based on size threshold. *Journal of vascular surgery.* 2013;58(6):1458-1466.
8. Troutman DA, Chaudry M, Dougherty MJ, Calligaro KD. Endovascular aortic aneurysm repair surveillance may not be necessary for the first 3 years after an initially normal duplex postoperative study. *Journal of vascular surgery.* 2014;60(3):558-562.
9. Skibba AA, Evans JR, Greenfield DT, Yoon HR, Katras T, Ouriel K, et al. Management of late main-body aortic endograft component uncoupling and type IIIa endoleak encountered with the Endologix Powerlink and AFX platforms. *Journal of vascular surgery.* 2015;62(4):868-875.
10. Lemmon GW, Motaganahalli RL, Chang T, Slaven J, Aumiller B, Kim BJ, et al. Failure mode analysis of the Endologix endograft. *Journal of vascular surgery.* 2016;64(3):571-576.
11. Type III Endoleaks Associated with Endovascular Graft Systems - Letter to Health Care Providers. 2017; https://www.fda.gov/MedicalDevices/Safety/LetterstoHealthCareProviders/ucm577859.htm. Accessed February, 2018.
12. England A, Garcia-Finana M, McWilliams RG. Multicenter retrospective investigation into migration of fenestrated aortic stent grafts. *Journal of vascular surgery.* 2015;62(4):884-892.
13. Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Goldberg RJ, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. *Circulation.* 2011;123(24):2848-2855.

Legends

Figure 1
The Cook Zenith Fenestrated graft is composed of a proximal main body (a) and a distal bifurcated piece (b). Main body proximal diameter ranges from 24 – 36 mm and house up to three modifications consisting of fenestrations or scallops. The available length of the distal main body is dependent on the proximal diameter. Regardless, the junctional diameter between the proximal and distal pieces are set at a diameter of 24 mm, respectively. The maximum available overlap between the two stents should be pursued for the individual patient.

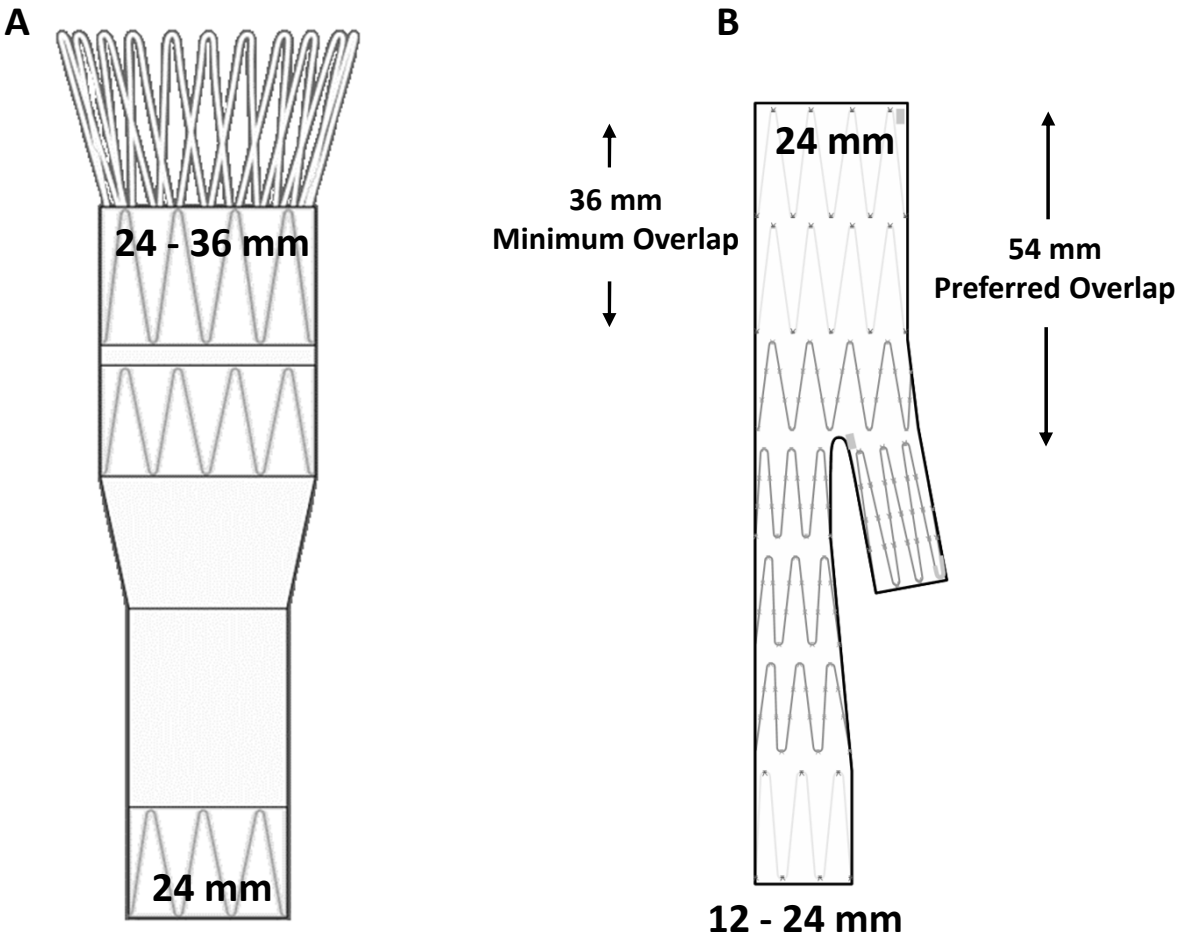
Figure 2
A three-dimensional reconstruction was performed (a) demonstrating the loss of junctional apposition between the proximal and distal aortic pieces resulting in a type III endoleak (arrowhead). In (b) and (c), coronal and sagittal views demonstrate the same anatomy.

Figure 3
An iliolumbar collateral (a, arrow) was feeding the residual sac causing pressurization and sac expansion. A right iliac limb was implanted to treat a type Ib endoleak (b). After continued sac expansion, another hypertrophied iliolumbar was embolized (c).

Figure 4
Increasing aortic angulation in the setting of a type Ib endoleak resulted in complete junctional separation (arrows) between the proximal main body and distal bifurcated stent (a, b).

Table 1
ZFEN characteristics associated with the individual patients.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Proximal Diameter	32 mm	32 mm	36 mm	32 mm	28 mm
Iliac Diameter	20 mm	24 mm	24 mm	24 mm	24 mm
Initial Angulation >45°	Yes	Yes	No	Yes	Yes
Initial Junctional Overlap	55 mm	50 mm	40 mm	35 mm	55 mm
1-Year Overlap	53 mm	38 mm	40 mm	26 mm	50 mm
2-Year Overlap	50 mm	30 mm	40 mm	14 mm	46 mm
3-Year Overlap	37 mm	30 mm	IIIa Endoleak	N/A	37 mm
4-Year Overlap	IIIa Endoleak	N/A	N/A	N/A	IIIa Endoleak
Time to Type Ib Endoleak	45 months	24 months	34 months	20 months	6 months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24 - 36 mm
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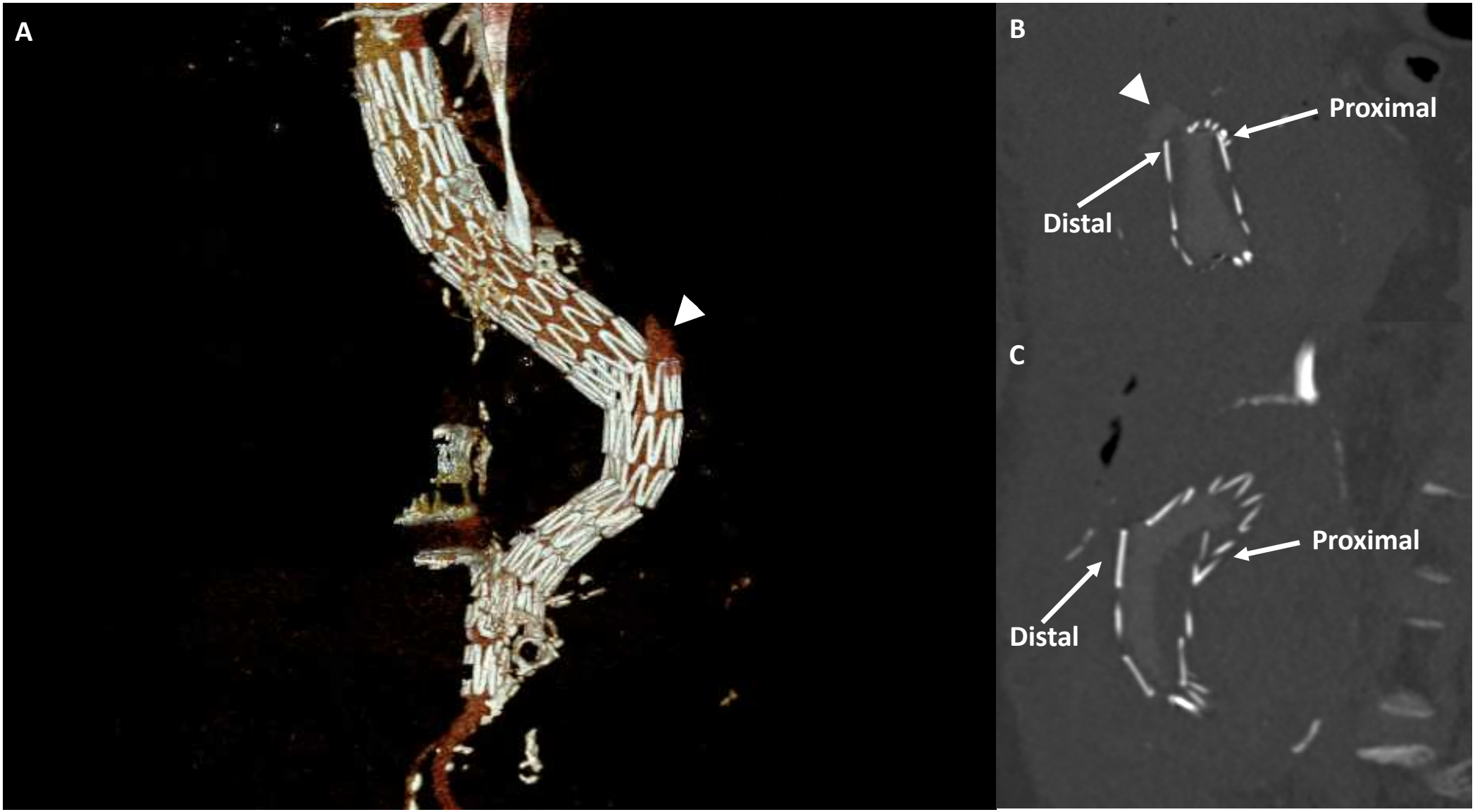
Preferred Overlap
12 - 24 mm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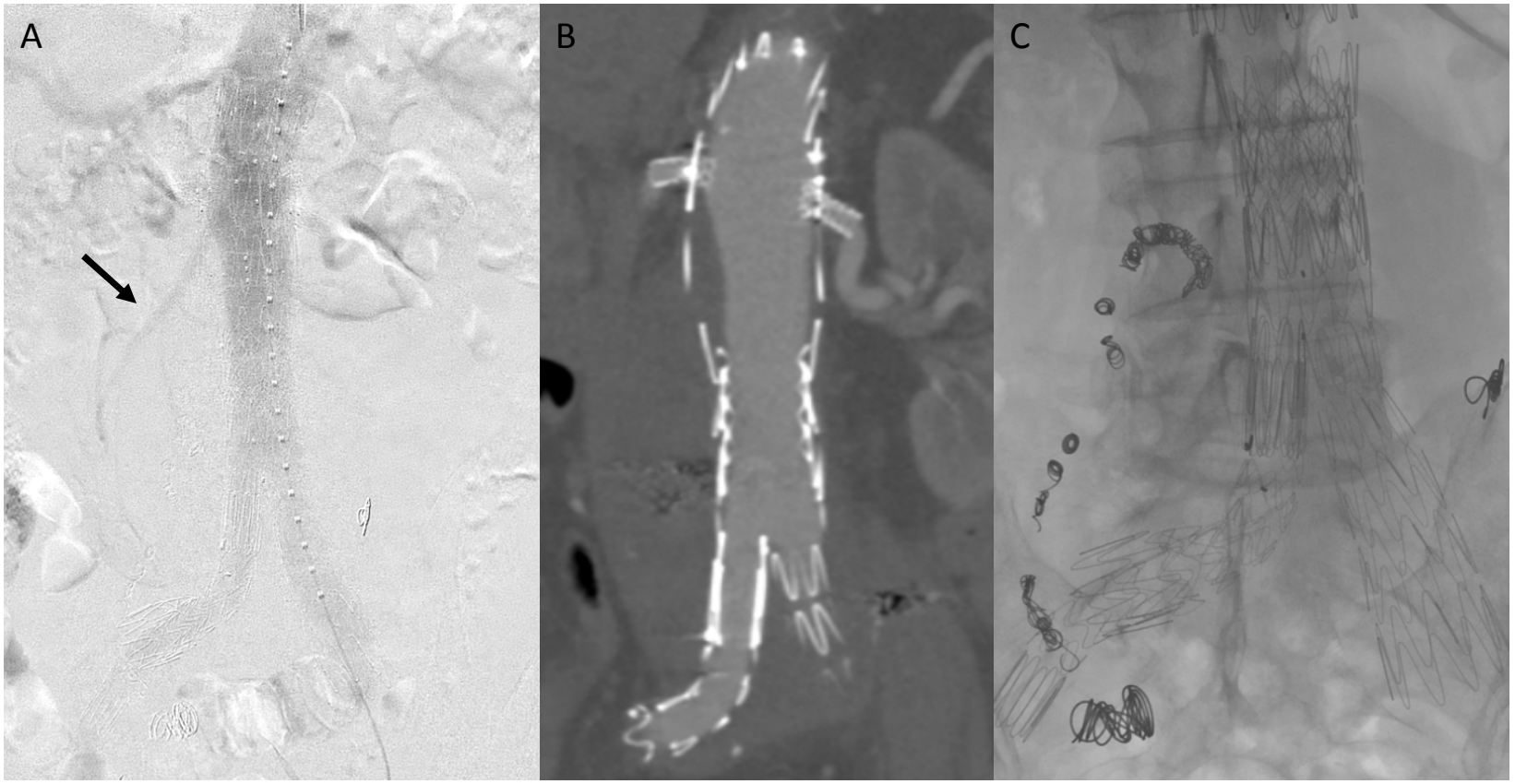
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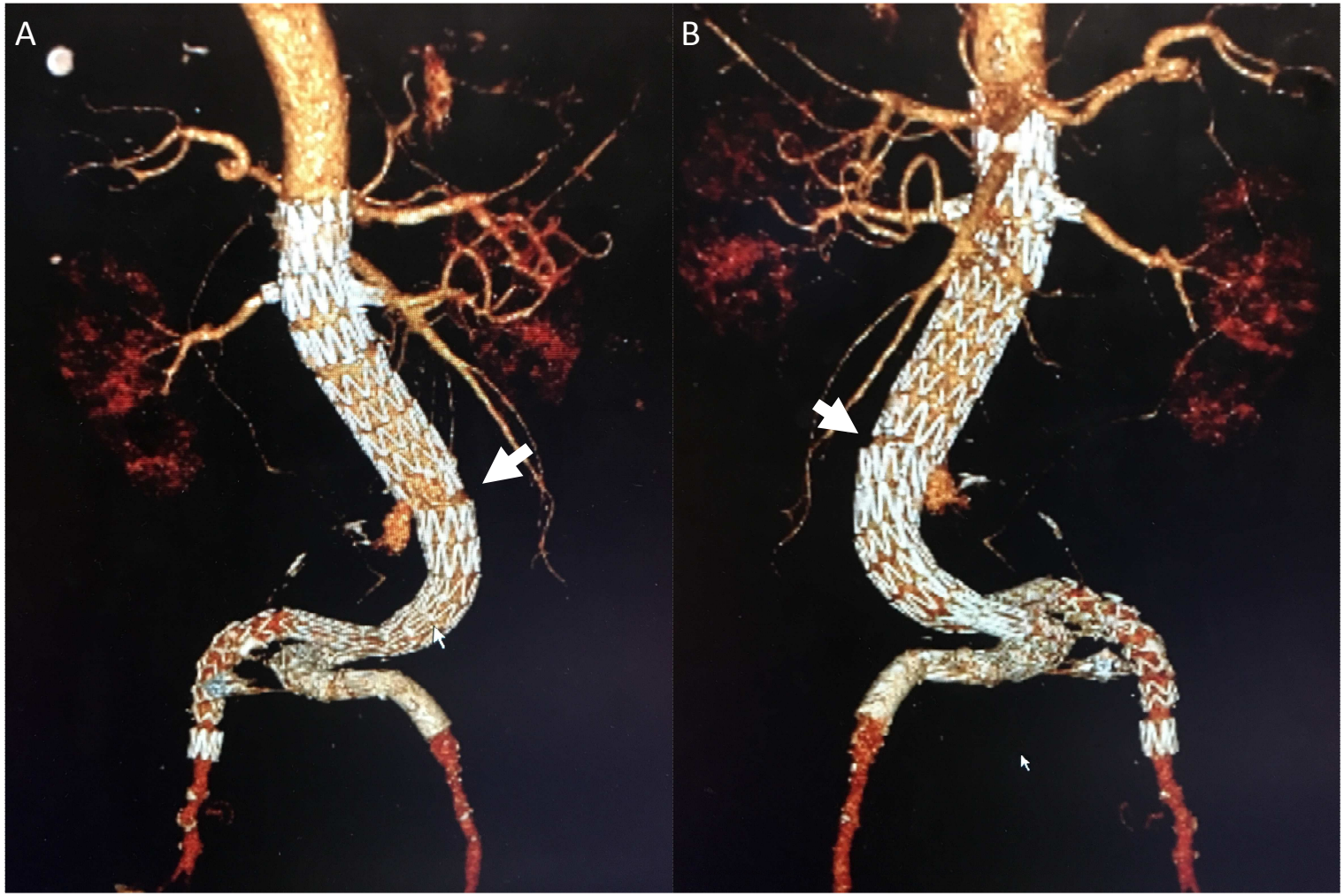
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