

# Adverse events associated with AXIOS stents: Insights from the manufacturer and user facility device experience database

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## ABSTRACT

**Background and Objectives:** The AXIOS stent is indicated for transgastric or transduodenal drainage of symptomatic pancreatic pseudocysts and symptomatic walled off necrosis. The AXIOS stent functions as a conduit which allows solid and liquid pancreatic fluid collections (PFC) contents to pass into the luminal GI tract and also allows the passage of standard and therapeutic endoscopes into the PFC to perform endoscopic debridement. We aim to investigate the number and type of complications associated with AXIOS stents. **Materials and Methods:** We analyzed postmarketing surveillance data from the Food and Drug Administration Manufacturer and User Facility Device Experience (MAUDE) database January 2016 to February 2021. **Results:** During the study period, approximately 588 reports with 579 device issues and 250 patient complications were identified. Most device complications were due to stent positioning problems or stent malpositioning ( $n = 206$ ; 35.6%), followed by stent migration ( $n = 72$ ; 12.4%), premature deployment ( $n = 61$ ; 10.5%), material integrity ( $n = 56$ ; 9.6%), deployment failure ( $n = 47$ ; 8.1%), and difficulty removing the stent ( $n = 45$ ; 7.7%). The most reported patient adverse events were hemorrhage/bleeding ( $n = 81$ ; 32.4%), perforation ( $n = 26$ ; 10.4%), pain ( $n = 22$ ; 8.8%), unspecified infection ( $n = 20$ ; 8.0%), and death ( $n = 17$ ; 6.8%). **Conclusions:** Findings from the MAUDE database highlight patient and device complications which endoscopists should be aware of before AXIOS stent placement.

**Key words:** AXIOS stent, endoscopy, pancreatic fluid collection

## INTRODUCTION

A novel large-diameter self-expanding metal stent with bilateral flanges, the AXIOS stent (Boston Scientific, Natick, MA, USA), has been designed

especially for transmural drainage of pancreatic fluid collections (PFCs) including pancreatic pseudocysts and walled-off pancreatic necrosis (WON). The stent has

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been widely adopted for this indication and is used in the United States and around the world.<sup>[1-4]</sup>

The AXIOS stent is silicone covered with a nitinol-braided design which is deployed under EUS guidance, with or without the assistance of fluoroscopy.<sup>[3]</sup> The AXIOS stent has a “dumbbell-shaped” configuration which allows for wide flanges on both ends. This helps to prevent stent migration by providing an anchoring point and even distribution of pressure on the luminal walls within the PFC.

The AXIOS stent is indicated for transgastric (TG) or transduodenal (TD) drainage of symptomatic pancreatic pseudocysts ( $\geq 6$  cm in size) and symptomatic WON ( $\geq 6$  cm in size with  $\geq 70\%$  fluid content) that are adherent to the gastric or bowel wall.<sup>[5,6]</sup> The AXIOS stent functions as a conduit which allows solid and liquid PFC contents to pass into the luminal GI tract and also allows the passage of standard and therapeutic endoscopes into the PFC to perform endoscopic debridement.

Multiple large-scale studies evaluating the AXIOS stent have demonstrated high clinical efficacy, but adverse events have been reported.<sup>[1-4]</sup> A large multicenter prospective cohort study demonstrated that EUS-guided placement of the AXIOS stent had a technical success rate of 98% (95% CI: 95%–100%), and a clinical success rate of 93% (95% confidence interval [CI]: 77%–100%) for pancreatic pseudocysts and 81% (95% CI 69%–94%) for pancreatic walled off necrosis (WON), respectively.<sup>[7]</sup> However, the adverse event rate in this study was 9% (95% CI: 2%–16%), which included perforation and PFC infection.<sup>[7]</sup> In addition, a multicenter, international, retrospective review from 15 centers on patients who underwent placement of learning activity management system (LAMS) for the management of PFCs reported that seventy-nine LAMS-related adverse events occurred in 74 of 304 patients (24.3%), after a mean time of 25.3 days (median, 18 days; interquartile range: 6–30).<sup>[3]</sup> Another multicenter, retrospective study involving 14 centers of patients who underwent EUS-guided drainage of WON found that adverse events were observed in 9.8% of LAMS and these were rated as severe in 2.0% of cases.<sup>[8]</sup>

The aim of this study was to evaluate events associated with the use of the AXIOS stent through the Food and

Drug Administration (FDA’s) Manufacturer and User Facility Device Experience (MAUDE) database from 2016 to 2021.

## MATERIALS AND METHODS

We analyzed postmarketing surveillance data on AXIOS stents from the FDA MAUDE database to report device-related deaths, injuries, and modes of failure. The MAUDE database collects major adverse reports involving medical devices after FDA approval. Reporting can be mandatory (manufacturers, importers, and device-user facilities) or voluntary (healthcare professionals, patients, and consumers) and is freely and publicly accessible, see website: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search>. Cfm.

The database is updated monthly with medical reports containing information on the device, event date, whether the device was returned to the manufacturer, and users’ and manufacturers’ event narratives. Events are classified on the basis of severity into four categories: death, injury, malfunction, or other. If a device is deemed defective, the FDA can issue safety alerts or recalls. Although this surveillance system cannot be used to establish definitive event rates, it can provide important insights into the most encountered complications and into potential mechanisms of medical devices.

We queried the MAUDE database from January 2016 to February 2021. Individual reports were analyzed for date, device issues, and patient adverse including intensive care unit (ICU) admission, treatment, and mortality. Statistical analysis was performed using SPSS statistics version 27 (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). No IRB approval needed for this study as the MAUDE Database is publicly accessible and deidentified.

## RESULTS

Five hundred and eighty-eight reports with 579 device issues and 250 patient complications were identified. During the study period, the number of adverse events reported to the FDA increased from 17.2% to 24.5% in 2020. Most device complications were due to a stent positioning problems or stent malpositioning ( $n = 206$ ; 35.6%), followed by stent migration ( $n = 72$ ; 12.4%), premature deployment ( $n = 61$ ; 10.5%), material integrity ( $n = 56$ ; 9.6%), deployment failure ( $n = 47$ ; 8.1%), and difficulty removing the

stent ( $n = 45$ ; 7.7%). Other less frequent device issues are reported in Table 1.

The most reported patient adverse events were hemorrhage/bleeding ( $n = 81$ ; 32.4%), perforation ( $n = 26$ ; 10.4%), pain ( $n = 22$ ; 8.8%), unspecified infection ( $n = 20$ ; 8.0%), and death ( $n = 17$ ; 6.8%). Other less frequently reported patient adverse events are reported in Table 2. Eight patients (1.4%) required ICU level of care, though unclear if due to underlying systemic disease or related to the stent only.

Device problems and patient complications were further characterized according to the location of endoscopic placement (*e.g.* TG position and TD position). Approximately 332 (56.4%) reported adverse event cases reported using TG positioning, while 64 (10.9%) reported adverse event cases reported TD positioning; 192 (32.7%) cases did not provide sufficient data to be categorized according to endoscopic placement [Tables 3 and 4]. TG was associated with a higher stent positioning problem compared to TD (TG 116 vs. TD 36); as well as higher bleeding events (TG 48 vs. TD 0).

## DISCUSSION

We performed an analysis of the FDA MAUDE database for adverse events and device problems related to AXIOS stent placement. Hemorrhage/bleeding, perforation, pain, unspecified infection, and death were the most frequently reported adverse events. Stent positioning problems, migration or expulsion, premature deployment, and problems with material integrity leading to malfunction were the most frequently reported device problems.

Unsurprisingly, deployment of the AXIOS stent in the TG position accounted for most reported complications (as PFCs are typically retrogastric). It should be noted that TD positioning of the AXIOS stent was utilized far less frequently, which may account for its lower rate of reported complications. To date, there are no head-to-head randomized clinical trials comparing the safety and efficacy of TG versus TD endoscopic placement of the AXIOS stent. This may be because the site chosen for cystenterostomy is made clinically based on the characteristics of the PFC, and the preference of the operator and likely cannot be randomized.<sup>[9]</sup>

**Table 1. Device issues reported**

Device problem	<i>n</i>
Entrapment of device	16
Electrical problem	6
Difficult to advance	11
Material integrity	56
Position problem	206
Partial blockage	25
Migration or expulsion	72
Premature activation	61
Detachment of device component	29
Difficult to remove	45
Activation failure	47
Operates different than expected	4
Device contaminated	1

NOS: Not otherwise specified

**Table 2. Adverse events reported**

Adverse events	<i>n</i>
Edema	1
Hematoma	3
Fistula	2
Syncope	1
Erosion	12
Abscess	2
Fever	10
Pain	22
Nausea	2
Vomiting	6
Perforation	26
Unspecified infection	20
Peritonitis	8
Sepsis	4
Obstruction	6
Laceration	3
Cardiac arrest	1
Pneumonia	3
Abdominal distension	1
Dyspnea	1
Death	17
Aneurysm/pseudoaneurysm	9
Hemorrhage/bleeding	81
Shock	2
Thrombus	1
Jaundice	3
Stenosis	3

NOS: Not otherwise specified

A substantial amount of literature exists supporting the clinical utility of the AXIOS stent. Small retrospective studies have demonstrated that the AXIOS stent has a higher technical success rate (98.9%) when compared to fully covered self-expanding metal stents and double pigtail stents.<sup>[2,10-12]</sup> These studies also concluded that the AXIOS stent achieves a PFC clinical resolution rate in

92.5% of cases.<sup>[2,10-12]</sup> The reported complication rate in these studies ranged from 5% to 9.4%.<sup>[2,10-12]</sup>

AXIOS stents have been widely used for a variety of pancreatic and off-label nonpancreatic indications. These included but not limited to biliary drainage (EUS-guided choledochoduodenostomy and EUS-guided cholecystostomy), luminal

bypass (EUS-guided gastroenterostomy), EUS-guided transmural drainage of PFCs (including walled off necrosis and pseudocysts), and for treatment of postsurgical fluid collections.<sup>[13-18]</sup> Table 5 shows a summary of these indications and their rates technical and clinical success as well as adverse events. Overall, AXIOS stent placement has been associated with high clinical and technical success with adverse events ranging from 4% to 22%, depending on the indication. These results indicate that adverse events are significant and should be carefully reviewed between endoscopist and patient before stent placement.

A multicenter, international, retrospective review concluded that the adverse events associated with LAMS are not negligible and should be considered before utilized for the drainage of PFCs.<sup>[3]</sup> However, while the placement of AXIOS stents is associated with risks, AXIOS stents appear to represent an overall safer and more effective approach when compared to percutaneous and surgical methods, and endoscopic drainage of pancreatic pseudocysts and necrosis is, and will likely remain, first-line therapy.<sup>[19]</sup>

**Table 3. Device issues reported according to position**

Device problem	Transgastric	Transduodenal	Unspecified
Entrapment of device	10	2	4
Electrical problem	4	2	0
Difficult to advance	5	1	5
Material integrity	30	6	20
Position problem	116	36	54
Partial blockage	13	0	12
Migration or expulsion	38	5	29
Premature activation	32	8	21
Detachment	16	1	12
Difficult to remove	28	2	15
Activation failure	27	6	14
Unexpected operation	1	2	1
Device contaminated	1	0	0

NOS: Not otherwise specified

**Table 4. Adverse events reported according to position**

Adverse events	Transgastric	Transduodenal	Unspecified
Edema	1	0	0
Hematoma	2	0	1
Fistula	1	0	1
Syncope	0	0	1
Erosion	5	0	7
Abscess	1	0	1
Fever	6	1	3
Pain	9	3	10
Nausea	2	0	0
Vomiting	3	1	2
Perforation	10	1	15
Unspecified infection	7	3	10
Peritonitis	2	1	5
Sepsis	3	1	0
Obstruction	2	0	4
Laceration	2	0	1
Cardiac arrest	1	0	0
Pneumonia	0	0	3
Abdominal distension	0	1	0
Dyspnea	1	0	0
Death	6	2	9
Aneurysm/pseudoaneurysm	4	0	5
Hemorrhage/bleeding	48	0	33
Shock	1	0	1
Thrombus	0	0	1
Jaundice	0	0	3
Stenosis	0	0	3

NOS: Not otherwise specified

**Table 5. Indications and outcomes of lumen apposing metal stent placement**

Type of study	Number of patients	Indication for LAMS	Technical success (%)	Clinical success (%)	Adverse events (%)	Reference
Meta-analysis	737	Pancreatic walled off necrosis	-	88.5% (95% CI 82.5-92.6)	11.2% (95% CI 6.8-17.9)	Mohan et al.
Meta-analysis	332	Pancreatic pseudocysts	95.76%	94.06%	-	Lyu et al.
Meta-analysis	1437	Biliary drainage	91.5% (95% CI 87.7-94.2)	87% (95% CI 82.3-90.6)	17.9% (95% CI 14.3-22.2)	Dhindsa et al.
Meta-analysis	278	Palliation of gastric outlet obstruction	95.2% (CI 87.2-98.3)	93.3% (CI 84.4-97.3)	10.7% (CI 4.3-24.5)	Chandan et al.
Meta-analysis	1538	Symptomatic gallbladder disease	94.65% (95% CI 91.54-96.67)	92.06% (95% CI 88.65-94.51)	11.71% (95% CI 8.92-15.23)	McCarty et al.
Retrospective	46	Malignant distal biliary obstruction	93.5%	97.7%	11.6%	Anderloni et al.
Multicenter retrospective	47	Postsurgical fluid collections	93.6%	89.3%	4.25%	Mudireddy et al.

CI: Confidence interval; LAMS: Lumen-apposing stent

Our analysis of the MAUDE database revealed 81 patients who experienced hemorrhage/bleeding associated with AXIOS stent placement or removal. The mechanism by which AXIOS-related hemorrhage occurs is the subject of significant discussion and controversy. A majority of the reports described significant hemorrhage of the splenic artery either during endoscopic placement or upon stent removal. 81 of the 81 [100%] patients who experienced hemorrhage/bleeding underwent AXIOS stent placement in the TG position. It is believed that the intimate anatomical relationship of the splenic artery and posterior gastric wall may contribute to the heightened adverse events reported in the TG position. Furthermore, many patients with severe pancreatitis develop splenic and/or portal vein thrombosis and collateral vasculature in the retroperitoneum that could also be sources of bleeding.

Our study showed that there were perforations ( $n = 26$ ), pain ( $n = 22$ ), and unspecified infections ( $n = 20$ ) following AXIOS stent placement. Importantly, we also identified 17 deaths during the study period. It must be noted that, at this time, there is limited information available regarding these deaths, and patients with pancreatic pseudocysts and/or pancreatic necrosis represent a high-risk patient cohort.

There are several limitations to this study: (1) MAUDE database reporting is inconsistent, and complications may be underreported; (2) details regarding procedures are limited, making it difficult to establish the exact cause of the reported events, such as operator error, interaction with other devices, or device defect; (3) the total number of reported devices used by the reporting

facility or from the manufacturer during the research time frame is unavailable, so the incidence of adverse events cannot be estimated; and (4) MAUDE database does not report the total number of AXIOS stent placements performed annually in the United States.

## CONCLUSIONS

AXIOS stent placement is widely performed for the drainage of PFCs. Our analysis of the FDA MAUDE database revealed the type, number, and trends of reported device adverse events. Endoscopists should be aware of the risk of hemorrhage/bleeding, perforation, pain, and infection as potential major complications of Axios stent placement.

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### *Conflicts of interest*

Douglas G. Adler is an Co-Editor-in-Chief of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of this editor and his research groups.

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