Post-cystoscopy infections and device malfunctions in reprocessed flexible cystoscopes in a national database

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Introduction: *Flexible cystoscopes can be multi-use devices that visually inspect genitourinary structures such as the bladder and urethra. The objective of this study is to characterize the adverse events and associated device malfunctions of reusable flexible cystoscopes and to provide information on contamination and post-procedural infections.*

Materials and methods: *The Manufacturer and User Facility Device Experience (MAUDE) database was queried for all adverse events and device malfunctions related to the use of flexible cystoscopes between January 2015 and December 2020. The MAUDE adverse event classification system was used to standardize the severity of complications and special focus was taken to identify clusters of events related to a single device.*

Results: *A total of 335 adverse events related to flexible cystoscopes were identified. Most adverse events associated with patient harm were caused by infection (n = 121), which included 19 cases of sepsis, one ICU admission, and one death. Among the infections, 29 cases showed growth of the same organism in both the device and patient. There were five infectious outbreaks identified and each outbreak was attributed to a single cystoscope. Other adverse events included mechanical malfunction (n = 6) and allergic reaction (n = 1).*

Conclusions: *Our findings highlight the risk of post-procedural infection associated with flexible cystoscope contamination. Further studies are needed to characterize the prevalence and incidence of flexible cystoscope contamination and to develop strategies to prevent post-procedural infection.*

Key Words: flexible cystoscopy, adverse events, MAUDE, device malfunction, infection

Introduction

Flexible cystoscopy is thought to carry such low risk of infection that routine use of antibiotics is not recommended in healthy asymptomatic adults.[1,2] However, in April 2021, the US Food and Drug Administration (FDA) released a statement to health care providers on the risks of infection from reprocessed urological endoscopes.[3] Since 2017, the FDA has reported over 450 medical device reports (MDRs) involving post-procedural infections or other potential contamination sources associated with cystoscopes and ureteroscopes. The FDA has initiated an investigation to identify potential causes of contamination such as device design, reprocessing methods, and instructions in the labeling. As a result of this investigation, Karl Storz issued a medical device recall notice in April 2022 for certain flexible, single channel endoscopes, including flexible cystoscopes, and removed high-level disinfection as an authorized sterilization method.[4] The urologic community is now in need of further information regarding scope contamination and post-procedural infection.

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The Manufacturer and User Facility Device Experience (MAUDE) database is a national database managed by the FDA that offers insight into these events. Through the MAUDE database, MDRs are anonymously submitted to the FDA by both mandatory and voluntary reporters. Mandatory reports consist of manufacturers, importers, and device user facilities while voluntary reports consist of health care professionals, patients, and consumers. These reports are used in post-market surveillance to detect any potential device-related safety issues. In this study, we characterize the adverse events and associated device malfunctions related to the use of flexible cystoscopes with the goal of providing further information on contamination and post-procedural infection.

Materials and methods

The MAUDE database was queried using the terms "flexible cystoscope" and "flexible cystourethroscope" to gather all adverse events reported between January 1, 2015 and December 31, 2020. The following details of each MDR were collected: the name of the manufacturer, the source of the report (mandatory versus voluntary), the reporter country code, the device problem, and the patient complication. If a single device was implicated in multiple adverse events, the report numbers of all involved MDRs as listed in each report were cross-referenced.

In any event that resulted in infection or contamination, the following details were noted: the presence of any device-related factors, the type of microorganism involved, and if present in either the subject device or the patient sample. A validated classification system developed for the MAUDE database by Gupta et al was used to characterize the adverse events as follows: level 1 (mild) – no harm occurring to the patient, level 2 (moderate) – harm to the patient requiring minor intervention, level 3 (severe) – harm occurring to the patient requiring major intervention, and level 4 (life-threatening event/death during procedure).[5]

Results

A total of 335 adverse events related to reusable flexible cystoscopes were reported in the MAUDE database. Most adverse events were considered level 1 (n = 203) and did not result in harm; however, 131 reports that resulted in patient harm, Table 1.

TABLE 1. **Severity and types of adverse events associated with flexible cystoscopies**

MAUDE adverse event classification	**Infection/contamination n (%)**	**Mechanical problem n (%)**	**Other n (%)**
Mild (I)	118 (48.6)	85 (93.4)	0 (0)
Moderate (II)	104 (42.8)	2 (2.2)	1 (100)
Severe (III)	19 (7.8)	4 (4.4)	0 (0)
Life-threatening or death (IV)	2 (0.8)	0 (0)	0 (0)
Total	**243 (100)**	**91 (100)**	**1 (100)**

TABLE 2. **Adverse events associated with patient harm (MAUDE level II-IV)**

Infection (n = 125)		**Mechanical malfunction (n = 6)**		**Hypersensitivity reaction (n = 1)**	
Unspecified/bacterial infection	104	Device entrapment requiring surgery	4	Allergic reaction	1
Sepsis	19	Difficult device removal	2		
ICU admission	1				
Death*	1				

*the exact relationship between the death to the subject device and infection is unclear. It is known that the subject device did not pass a leak test

TABLE 3. **Cystoscopy-related infectious outbreaks and associated reprocessing issues**

Date of device submission	#of patients	Bacterium isolated	Biofilm forming bacterium?	Improper reprocessing?	Passed leak test?	Mechanical damage?
1/2/2015	4	Pseudomonas	Yes	Unknown	Unknown	Unknown
6/14/2016	6	Salmonella	Yes	Unknown	Yes	Yes
10/1/2016	2	Pseudomonas	Yes	No	Unknown	No
9/18/2019	5	Proteus	Yes	Yes	Yes	Unknown
12/2/2020	9	E. coli	Yes	Yes	Unknown	Unknown

Each outbreak references the involvement of a single subject device that is cross-referenced in additional reports

Infection (n = 124) was the leading cause of adverse events associated with harm followed by mechanical malfunction (n = 6), and allergic reaction (n = 1). Most infections were described as 'unspecified or bacterial infection' (n = 103); however, 19 patients developed sepsis, one patient was admitted to the ICU and one patient died, Table 2. Table 2 also shows the mechanical complications associated with patient harm: 'difficulty removing device' (n = 2) or 'device entrapment requiring surgery' (n = 4). All six cases of mechanical complications described a malfunction of the device's angulation system. In the four cases of device entrapment requiring surgery, one case led to open surgery and the surgical approach in the other three cases was not specified.

Table 3 shows five separate infectious outbreaks involving 29 patients where the microorganisms found in the patient's samples matched those of the cystoscope's sample. Each of these outbreaks identified the involvement of a single cystoscope. The adverse events listed from these outbreaks were as follows: 'infection' (n = 24), sepsis (n = 9), 'hematuria' (n = 5), and 'urinary retention' (n = 4). Table 3 summarizes information on the type of microorganisms isolated and the associated cystoscope-related issues that were identified from each infectious outbreak.

The manufacturers identified were Olympus Medical System Corporation (n = 327) and Karl Storz Endovision (n = 8). Of the types of submissions, 334 were submitted mandatorily by the device manufacturers and one was submitted voluntarily by a risk manager. The number of reports submitted by country were as follows: United Stated (n = 182), France (n = 61), United Kingdom (n = 24), Canada (n = 14), Gambia (n = 8), Eswatini (n = 5), American Samoa (n = 4), New Zealand (n = 2), Austria (n = 1), Czech Republic (n = 1), and unspecified (n = 36).

Discussion

Our findings are suggestive of a relationship between improper reprocessing of cystoscopes and post-procedural infections. Using the MAUDE database, we identified five separate infectious outbreaks attributed to the use of a single flexible cystoscope. To our knowledge, there are only five infectious outbreaks attributed to cystoscope contamination in the medical literature, with four outbreaks involving multi-drug resistant pathogens.[6-10] In our study, we identified 19 cases of sepsis, one ICU admission, and one death related to flexible cystoscopy use. Our results highlight the underreported nature of infections caused by cystoscope contamination and how contamination can lead to dangerous outcomes.

Although flexible cystoscopes are safely reused in the vast majority of cases, they may be prone to wear and tear, which can be difficult to recognize. Our study shows how device malfunctions have the potential to cause catastrophic outcomes such as the need for emergent surgery in the setting of mechanical failure. To our knowledge, these are the first reports of flexible cystoscope malfunction leading to surgical intervention. In light of these findings, one may consider performing regular testing and scheduled maintenance of reusable devices. In addition, damage to the working channels of endoscopes has been shown to favor bacterial colonization and the formation of biofilms that can be difficult to eradicate with standard sterilization protocols.[11] Importantly, as shown in Table 3, we were able to identify that all of the cystoscopy-related outbreaks were associated with pathogens capable of forming biofilms. Given the difficulty in eliminating biofilm-producing bacteria, perhaps routine device microbiological testing should play a role in ensuring appropriate quality control. Practices of endoscope sampling and culturing are

encouraged by manufacturers such as Olympus as a means to detect contamination before a device for patient examination.[12] Performing regular quality assurance protocols of device sampling and culturing may be useful in identifying errors in reprocessing as well as detecting endoscope damage if persistent positive cultures are seen with a single device.

In April 2022, the FDA released a statement instructing cystoscope users to discontinue liquid chemical sterilization or high-level disinfection methods due to their suboptimal reprocessing.[13] The American Urological Association (AUA) guidelines for reprocessing flexible cystoscopes do not yet reflect the recent statement by the FDA regarding the discontinuation of liquid chemical sterilization or high-level disinfection.[14] In addition, the AUA guidelines do not mention the role of sampling and culturing endoscopes to detect contamination. In light of the FDA's recent report and Karl Storz's medical device recall notice, there is a clear need to develop strategies to prevent as well as identify endoscopic contamination. We may expect to see more manufacturers release similar statements to avoid the use of inadequate reprocessing techniques.

The strength of this study is its large sample size and the ability to examine rare adverse events. We identified several infectious outbreaks linked to a single device and described the associated device malfunctions. We demonstrated that device-contamination is a global phenomenon. Also, we reported adverse events related to flexible cystoscopes that led to emergent surgery. There are, however, several limitations to the data. First, it is difficult to ascertain the true proportion of adverse events when compared to total number of cystoscopic cases as this information is not available in the MAUDE database. Additionally, the database does not provide clinical granularity such as comorbidities or details of a procedure. Since adverse events are reported both mandatorily and voluntarily, the true incidence of any post-cystoscopy complication cannot be calculated. Prior literature estimates around 1 million cystoscopies are performed annually in the United States.[15] Although the true incidence remains unknown through the MAUDE database, a rough estimate can be extrapolated with this information. Furthermore, it can be difficult to determine the etiology of an adverse event, such as why a particular cystoscope became contaminated. As noted in Table 2, over half of device related UTIs did not have an identifiable cause. Lastly, it is also possible that a patient had a UTI before the cystoscopy was conducted.

In recent years there has been growing interest for single-use endoscopes. Single-use devices eliminate the contamination risks and costs of reprocessing, though the economic benefit can vary greatly depending on practice size and volume.[16-18] To our knowledge, there are no studies that compare the post-procedural complication rates such as UTIs of single use versus standard reusable endoscopes which can be an area of focus for future studies. Finally, the urological community may benefit from standardized practices for cystoscopic maintenance, reprocessing, and contamination testing.

Conclusions

Our findings highlight the risk of post-procedural infection associated with flexible cystoscope contamination as well as associated device malfunctions. Further studies are needed to characterize the prevalence of flexible cystoscope contamination and to develop strategies to prevent post-procedural infection and device mechanical failures. □

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