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The management of endoscopic retrograde cholangiopancreatography-related infections risk: results of an italian survey at regional level

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Parole chiave: ERCP, infezioni associate al duodenoscopio, rischio infettivo, prevenzione delle infezioni.

Abstract

Background and aim. *Among the Endoscopic retrograde cholangiopancreatography (ERCP) adverse events, an increasingly arising problem is the transmission of Multi Drug Resistant (MDR) Bacteria through duodenoscopes. The aim of this survey was to evaluate the current clinical practice of management of ERCP associated infections in Emilia-Romagna, Italy.*

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Methods. *An online survey was developed including 12 questions on management of ERCP associated infections risk. The survey was proposed to all 12 endoscopy centers in Emilia Romagna that perform at least > 200 ERCPs per year.*

Results. *11 centers completed the survey (92%). Among all risk factors of ERCP infections, hospitalization in intensive care units, immunosuppressant therapies, and previous MDR infections have achieved a 80 % minimum of concurrence by our respondents. The majority of them did not have a formalized document in their hospital describing categories and risk factors helpful in the detection of patients undergoing ERCP with an high-level infective risk (9/11, 82%).*

Most centers (8/11, 72%) do not perform screening in patients at risk of ERCP infections. Post procedural monitoring is performed by 6 of 11 centers (55%).

Conclusion. *Our survey showed that, at least at regional level, there is a lack of procedures and protocols related to the management of patients at risk of ERCP infections.*

Introduction

Endoscopic retrograde cholangio-pancreatography (ERCP) is an accepted method in the management of benign and malignant bilio-pancreatic diseases (1). Although ERCP is in general effective and safe, it could be associated with several recognized adverse events, including post-ERCP pancreatitis (PEP), hemorrhage, cholangitis, cholecystitis, perforation, and cardiopulmonary events (2). Among these adverse events, there is the transmission of Multi Drug Resistant (MDR) bacteria through the use of contaminated duodenoscopes (3), which is an increasingly arising issue.

Previous data showed that post-ERCP infective complications can reach 5% (e.g. ascending cholangitis and cholecystitis) (4), but the range of infections transmitted through duodenoscopes can vary between 0.4% and 1% (5-6). In 2001, the American Society of Gastrointestinal Endoscopy (ASGE) reported 1 case of pathogen transmission for every 1.8 million endoscopic procedures performed (7).

Bacteria transmitted during ERCP are frequently MDR such as carbapenemics-resistant *Enterobacteriaceae* (*E. coli* and *Klebsiella spp*) or *Pseudomonas spp* and this results in a significant increase in mortality and morbidity in patients who contract these infections, compared to infections transmitted by susceptible organisms (3).

Infections transmitted through duodenoscopes are related to possible laps in reprocessing as well as to the structure of the duodenoscope (e.g., the elevator). Several studies have shown that the elevator area is difficult to clean with both automatic and manual disinfection procedures. (8). The contamination of endoscopes might depend on pathogen and surface factors, as well as environmental conditions (9). Furthermore, recent studies suggest that environmental contamination plays a significant role in Healthcare associated infections (HAIs) and in the unrecognized transmission of nosocomial pathogens during outbreaks, as well as ongoing sporadic transmission (10). Thus, despite the pivotal role of architecture of endoscopes, and the suggestion to shift to single use devices to reduce cross contamination, no randomized study has already confirmed that this solos strategy can impact substantially on reducing the overall risk. Furthermore, there is poor data regarding the identification and management of duodenoscopy-related infections, particularly in terms of patients at risk of infection and their correct reporting, as well as the pre- and post-procedural pathways. As a result, current practice mainly relies on expert opinion and personal preference. A guideline development requires the

knowledge of duodenoscope-associated infections "state of the art" in current clinical practice.

The aim of this survey was to evaluate the current clinical practice of management of duodenoscope-associated infections in one of the largest region of Italy, Emilia-Romagna, with regard to applied protocols and pathways and risk factors identification.

Methods

Study design

A regional online survey was conducted in Emilia-Romagna, a region in Northern Italy, including all the 12 centers of gastrointestinal endoscopy who perform at least 200 procedures per year.

The survey was developed by a regional core study team and consisted of 12 questions, divided into 2 domains: 1) Identification of patients at risk for duodenoscopy-associated infections, proper reporting, and specific pathways, 2) Pre-procedure screening and post-procedure monitoring of patients at risk of developing duodenoscopy-associated infections.

Risk factors for duodenoscopy-associated infections reported in the survey were based on studies published in the literature, respondents were not aware of this selection.

An online survey was built using Form Office. Invitations were sent through e-mail in July 2021. Additional reminders were sent in August and September 2021.

Statistical analysis

Only fulfilled survey responses were used for statistical analysis. Descriptive statistics have been used to analyze the data, using median and interquartile range (IQR) for non-normally distributed continuous variables and frequencies and percentages (%) for categorical variables. The statistical analyses were performed by the means of the statistical software SPSS version 25, Statistical Package for the Social Sciences, SPSS Inc., Chicago, Illinois.

Results

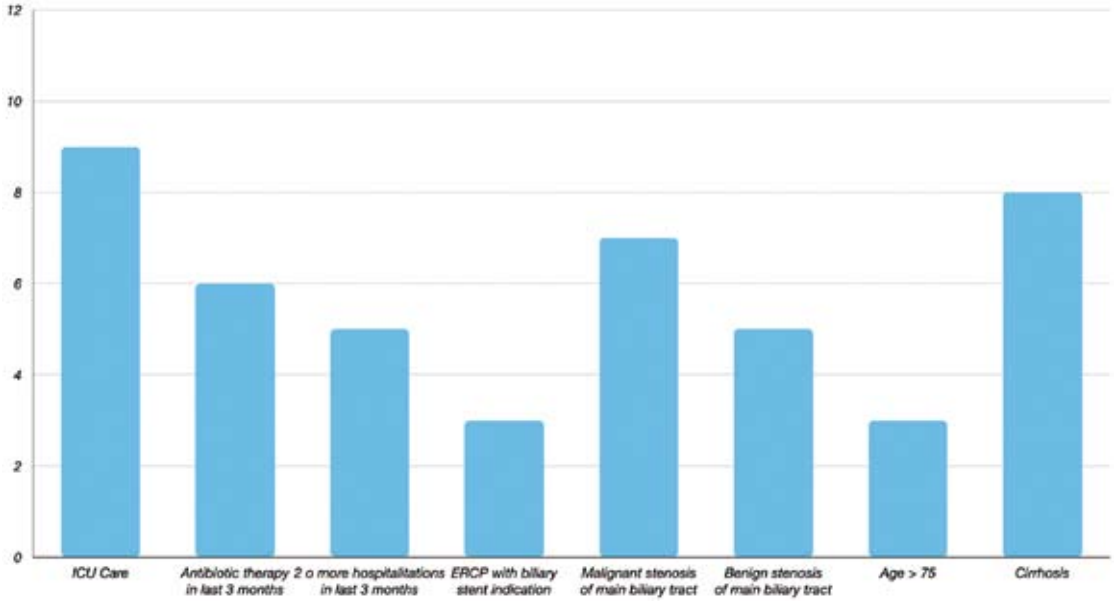
The survey was proposed to all 12 endoscopy centers performing ERCP (not less than 200 procedures/year) in Emilia Romagna, Northern Italy. 11 (92%) centers completed the survey. In Emilia Romagna these Endoscopy Units all together perform over 4,000 ERCPs per year.

Identification of patients at risk for duodenoscopy-associated infections, proper reporting, and specific pathways

Figure 1 A-B show the risk factors which are considered to be related to the possible development of duodenoscope-associated infections. To sum up, hospitalization in intensive care units, immunosuppressant therapies and previous MDR infections had more than 80% of agreement among respondents. Notably, most of the respondents neither have a formalized document in their hospital that describes the categories and risk factors for identifying patients undergoing ERCP as being at high-level infectious risk (9/11, 82%), nor a coded alert in the procedure request to identify these patients (10/11, 91%). In addition to that, 10 out of the 11 centers (91%) do not use a clinical register of patients at risk of duodenoscope infection. In 8 of the 11 centers (72%), there is no dedicated procedure for patients undergoing ERCP that are known to be MDR bacteria carriers, or any specific procedure defining the pathways of these patients (9/11, 82%). The results are shown in Table 1.

Pre-procedure screening and post-procedure monitoring of patients at risk of developing duodenoscopy-associated infections

As for pre-procedural screening in patients at risk of duodenoscope-related infections, most centers do not perform



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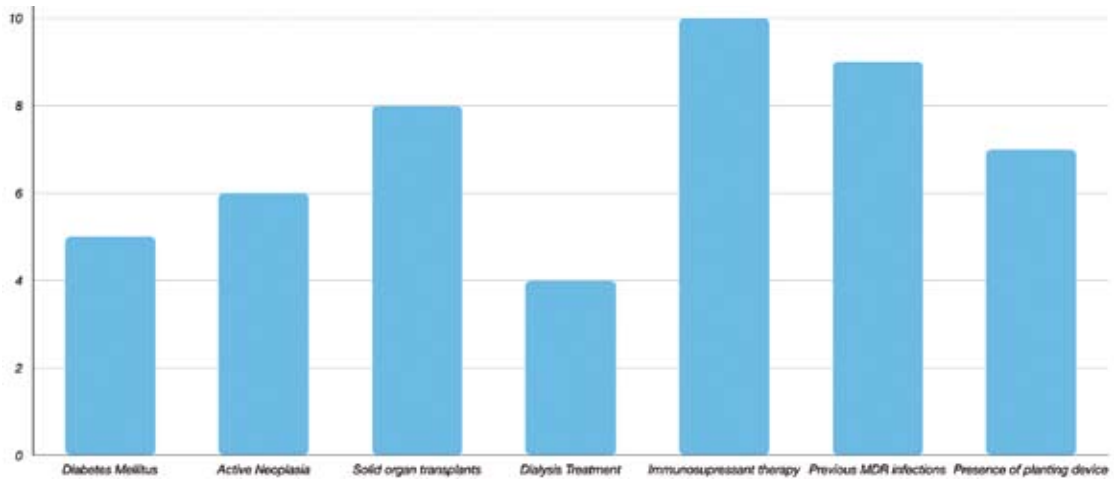

B

Figure 1A-1B - Risk factor associated to duodenoscope transmitted infections

screening at all (8/11, 72%), whereas only 3 centers perform rectal swabs for MDR bacteria. On the other hand, post procedural monitoring is performed by 6 of 11 centers (55%). In a great number of cases, with clinical and laboratory monitoring, only one center has confirmed to perform post-procedural rectal swabs at 3 days after ERCP and at the onset of symptoms. Finally, in most centers (8/11, 72%), there are no procedures/protocols for identifying suspected cross-contamination in cases of duodenoscopy-related infections. These results are presented in table 2.

Table 1 - Identification of patients at risk for duodenoscope-associated infections, proper reporting, and specific pathways.

Survey questions	No	Yes
Is there a formalized document at your center that describes the categories and risk factors for identifying patients undergoing ERCP as being at high risk for infection?	9 (82%)	2 (18%)
Is there an alert included in the ERCP exam request, formalized by specific procedure, that highlights and allows identification of patients at risk for infection?	10 (91%)	1 (9%)
Is there a clinical registry of patients at risk for infection in ERCP?	10(91%)	1(9%)
Is there a specific procedure for patients undergoing ERCP who are known to have infections?	8 (73%)	3 (17%)
Is there a specific procedure that defines the pathway for patients at risk of developing an ERCP infection?	9(82%)	2(18%)

Discussion and conclusions

The present survery seems to be, to our knowledge, the first one investigating the management of patients at risk of developing duodenoscope-related infections and we fiercely believe that it is noteworthy since it clearly identifies areas of intervention and improvement.

First of all, it has been shown that there is a lack of agreement on the alleged factors related to the risk of post-procedure infection. Indeed, only 3 factors (i.e., hospitalization in intensive care, immunosuppressant therapies, and previous MDR infections) have been marked by more than the 80% of the responders as *risk factors* for the development of duodenoscope-related infections (Figure 1). All the risk factors considered in the survey were extrapolated from those reported by specific studies. These, analyzed epidemic outbreaks as linked to the transmission of infection through the duodenoscope, yet they also included general risk factors for the development of nosocomial infections. In a study by Kim et al., published in 2016, following an outbreak of carbapenems-resistant *Enterobacteriaceae* (CRE) related to transmission by duodenoscopes, it emerged that some patient-related characteristics, such as recent antibiotic therapy (<180 days) and presence of cholangiocarcinoma, but also some procedure characteristics such as stent placement, are significantly associated with transmission of infections by duodenoscopes (8). In addition, other risk factors have

Table 2 - Pre-procedure screening and post-procedure monitoring of patients at risk of developing duodenoscope-associated infections

Survey questions	No	Yes
Is pre-procedural screening conducted for patients identified as being at risk for infection and undergoing to ERCP?	8 (73%)	3 (17%)
Is post-procedural monitoring conducted for patients at risk for ERCP infections?	5 (46%)	6 (54%)
In the case of post-procedural infection in ERCP, are there procedures/protocols for identifying suspected cross-contamination?	8(73%)	3(17%)

been reported regarding duodenoscope-transmitted infections, such as: more than 2 previous hospitalizations in the past 3 months; patients admitted to Intensive Care Unit (ICU); patients with benign/undetermined biliary tract stenosis (primary sclerosing cholangitis, PSC, autoimmune cholangitis) (11-13). Finally, the general risk factors for nosocomial infections by MDR bacteria reported in the literature, should also be considered, such as age > 75 years, patients with liver cirrhosis, diabetes, active neoplasms, chronic kidney disease requiring dialysis, solid organ transplant, or history of previous infections by MDR bacteria, permanent device carriers (14).

Nevertheless, it should be underlined that most of the published studies report only a descriptive case history and often the epidemic outbreak is not promptly identified, since they are retrospective evaluations. Therefore, the assessment of risk factors may also be biased, and this may explain why a complete agreement about the possible risk factors for duodenoscope-transmitted infections has not been reached, even among experts.

This lack of clear and well-established data can explain why most hospitals in our region have not implemented yet codified procedures of reporting patients at risk of developing duodenoscope-related infections or dedicated pathways. The absence of dedicated pathways and procedural alerts could facilitate transmission of MDR bacteria, in high-risk patients or asymptomatic carriers, regardless of the use of duodenoscopes.

In 2018, Suleyman et al. analyzed the role of environmental contamination in the transmission of nosocomial pathogens and healthcare-associated infections (HAIs) and concluded that in recent years there is an increasing link between the environmental contamination and the acquisition of nosocomial pathogens and HAIs, potentially leading to outbreaks and ongoing sporadic transmission. Indeed, although at least 25 separate outbreaks caused by contaminated duodenoscopes were identified worldwide between 2012 and 2015, affecting more than 250 patients (15-17), most of these outbreaks were not linked to any identifiable violation in disinfection and reprocessing protocols, and there was no apparent association with geographic location, manufacturer, or model of duodenoscopes (15). On the other hand, a recent meta-analysis published by Larsen et al., considering 15 studies with 925 contaminated duodenoscopes due to 13,112 samplings, shows that there is a 15.25% contamination rate of reprocessed patient-ready duodenoscopes (18).

As for the monitoring of patients at risk of duodenoscopy-transmitted infection, our survey shows that only 3 centers (27%) routinely perform procedural screening by rectal swabs. Our result is in line with a recently published survey by Thaker et al. (19), which showed that, out of the 244 participating centers, only 37 (15%) performed screening swabs for MDR bacteria. Therefore, it seems that monitoring of patients at risk for duodenoscope-associate infections is not integrant part of the Endoscopy service organization, and this gap should be promptly filled because it could also be a factor leading to transmission, in addition to procedural lapses in scope reprocessing.

Indeed, our survey shows that, although in more than half of the centers post ERCP monitoring is performed to identify possible infections with MDR bacteria related to the use of duodenoscopes, there are no standardized protocols on how to organize these checks or how to perform them. In fact, only 3 centers have procedures/protocols for the identification of suspected cross-contaminations in case of post ERCP infection.

We decided to include only the endoscopy services of the Emilia-Romagna region in this survey and this is clearly a limit

to the external validity of our findings. Furthermore, questionnaire-based surveys have inherent limitations about telling the truth. Thus, participants may have answered according to what they perceived to be correct rather than according to their practice introducing a response bias. However, given the paucity of data on this topic, our results are valuable.

Moreover, it should be noted that Emilia-Romagna is one of the largest regions of Italy and presents a highly efficient health-care system according to the "essential levels of care" (LEA, in Italian), therefore we believe that our results may be extended to most of Endoscopy services, at least of our country.

Our survey has several implications for research and practice. Since risk factors for post-ERCP infections have not been fully understood, large, prospective, multicenter, possibily international studies should be promoted on this issue. National and International Endoscopy Societies should promote education courses about this still neglected topic and propose standardized procedures and protocols to be adopted in Endoscopy services.

In conclusion, our survey showed that, at least at regional level, there is a lack of procedures and protocols related to the management of patients at risk of infections related to the use of duodenoscopes as well as their pre- or post-procedural screening. This fact could be an important cofactor to be considered regarding the transmission of MDR bacteria during ERCP. This survey identified areas of improvement that warrant prompt intervention.

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Riassunto

La gestione del rischio infettivo associato alla colangiopancreatografia endoscopica retrograda: risultati di un'indagine italiana a livello regionale

Introduzione ed Obiettivo dello studio. Tra gli eventi avversi della Colangiopancreatografia Endoscopica Retrograda (ERCP), un problema sempre più emergente è la trasmissione di batteri multi-resistenti (MDR) attraverso i duodenoscopi. L'obiettivo della presente indagine è stato quello di valutare l'attuale pratica clinica della gestione delle infezioni associate all'ERCP in Emilia-Romagna.

Metodi. È stato redatto un questionario online che comprendeva 12 domande sulla gestione dei pazienti a rischio di sviluppare infezioni associate all'ERCP. Il questionario è stato inviato a tutti i 12 centri di endoscopia dell'Emilia-Romagna che eseguono almeno più di 200 ERCP all'anno.

Risultati. 11 centri (92%) hanno completato il questionario. Tra tutti i fattori di rischio correlati al possibile sviluppo di infezioni in corso di ERCP; solo la degenza in terapia intensiva, le terapie immunosoppressive e precedenti infezioni da batteri MDR hanno raggiunto un minimo di 80% di concordanza tra i centri che hanno risposto. La maggior parte dei centri non ha un documento formalizzato nel proprio ospedale che descriva le categorie e i fattori di rischio utili per individuare i pazienti, sottoposti a ERCP, con un rischio infettivo elevato (9/11, 82%).

La maggior parte dei centri (8/11, 72%) non esegue lo screening nei pazienti a rischio di infezioni in corso di ERCP. Il monitoraggio post-procedurale viene effettuato da 6 centri su 11 (55%).

Conclusioni. La nostra indagine ha evidenziato come, almeno a livello regionale, mancano procedure e protocolli relativi alla gestione dei pazienti a rischio di infezioni in corso di ERCP.

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