

A Half Century of Endoscopic Retrograde Colangiopancreatography: Reflections of the Past, Present and Future

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The first endoscopic retrograde colangiopancreatography (ERCP) was performed half a century ago, and since then considerable advances have been achieved, this technique becoming the dominant endoscopic procedure for the management of many pancreaticobiliary diseases. Mostly used as a diagnostic method at the beginning, ERCP has become over the years almost entirely a therapeutic procedure in the management of biliary tract pathology, supplanting some surgical and percutaneous radiological procedures.

Professor C. Stanciu was fortunate enough to participate in the diagnostic and therapeutic ERCP procedures from their inception in Romania, witnessing the development of this revolutionary technique in the main university centers [1]. We considered it a duty to celebrate the 50th anniversary of ERCP by writing and publishing these brief reflections on the development of ERCP throughout its fascinating history and considering optimistically its future.

The early days. The first peroral cannulation of the bile and pancreatic ducts under fluoroscopic guidance was reported in 1965 [2] and the first endoscopic cannulation of the ampulla of Vater was reported in 1968 by William S. McCune [3]. He was an obstetrician, using a fiber duodenoscope with an external accessory channel taped

to the scope shaft as well as a balloon for cannulation [3]. In 1972, Peter Cotton described cannulation in 60 patients [4], and a year later, Meinhard Classen in Germany and Keiichi Kawai in Japan simultaneously performed the first biliary sphincterotomy [5, 6].

Ever onward. A significant and steady increase in the use of ERCP was observed worldwide between 1980-2000; in the United States alone the rate of ERCP nearly tripled [7]. The use of ERCP expanded in this period mainly as a diagnostic procedure. A decline in its use occurred after 2000 [7], due to the widespread availability of new, less invasive diagnostic methods: computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), and endoscopic ultrasound (EUS) [8].

How does the present look like? Therapeutic ERCP is used as a major endoscopic method in the management of pancreatic and biliary diseases, with more than 650,000 procedures per year only in the USA [9]. However, two important issues still remain to be solved: first, post-ERCP pancreatitis (PEP) prevention, and second, ERCP-related infections.

Prevention of post-ERCP pancreatitis. Pancreatitis remains the most frequent and severe complication of ERCP, occurring in 2-10% of unselected patients and in more than 15% of high-risk patients [10]. During the last two decades, a considerable effort has been made to reduce both the incidence and severity of PEP by pharmacologic and endoscopic techniques [11].

Pharmacologic prevention includes the use of nonsteroidal anti-inflammatory drugs (NSAIDs), hormones, sphincter of Oddi relaxants, and intravenous fluid administration. Early small studies evaluating rectal administration of either diclofenac [12] or indomethacin [13] reported a benefit in preventing PEP, and the European Society of Gastrointestinal Endoscopy recommended the use of rectal NSAIDs for the prevention of PEP [14]. Since then, several other studies and meta-analyses reported that NSAIDs significantly decreased the incidence of PEP and recommended rectally administered diclofenac or indomethacin before or closely after ERCP in every patient (without renal failure) undergoing this procedure [15].

Somatostatin and its synthetic analogue octreotide as well as sphincter of Oddi relaxants (nitrates, nifedipine, epinephrine and lidocaine) have been used with conflicting results in preventing PEP [16, 17]. Intravenous fluid administration with

lactated Ringer's solution or larger periprocedural fluid volumes has been proved to reduce the incidence and severity of PEP [18].

ERCP techniques refer to safe cannulation, guidewire cannulation, early precut biliary papillotomy, guided pancreatic duct access to facilitate difficult biliary cannulation (double-guidewire, pancreatic duct stent placement and transpancreatic sphincterotomy), or the use of large papillary balloon dilation.

Safe cannulation is influenced by several factors, such as papilla morphology, altered anatomy, operator's experience and the technique used. Patient selection is a critical step in preventing PEP [19]. Freeman et al. [20] showed that the rate of complications after ERCP with biliary sphincterotomy is primarily linked to the indication for the procedure and endoscopic technique, rather than to the patients' age and medical condition [20]. It should be underlined that successful cannulation represents the most efficient and safe approach to avoid PEP. In recent guidelines, there is now an accepted norm to limit the number of cannulation attempts before changing to alternate techniques [13, 21].

Standard cannulation techniques include guidewire assisted or contrast guided cannulation. Several randomized controlled trials and a meta-analysis demonstrated a significant improvement in the rate of bile duct cannulation by use of a guidewire [22, 23]. Therefore, based on such good evidence, expert endoscopists recommend guidewire cannulation when performing ERCP, but dye injection still has a role in difficult ERCPs to clarify anatomy and help gain access to the desired duct.

Pancreatic duct (PD) stents reduce the risk and probably the severity of PEP. As a general rule, in cases with high pre-ERCP risk of pancreatitis due to clinical or procedural factors, it is recommended to attempt to place a prophylactic PD stent [11].

Double guidewire technique could increase biliary cannulation rates without any additional risk for PEP, allowing the endoscopist to reassess CBD direction by keeping a partially occluded pancreatic duct [24].

Needle-knife sphincterotomy or precut biliary papillotomy can be used when other techniques for selective cannulation fail. Performed early after recognition of difficult cannulation situations, this technique would lower the risk of PEP [11, 25].

Transpancreatic sphincterotomy, although initially associated with higher rates of PEP, has recently been proven by several prospective studies as a safe procedure, allowing, in expert hands, rapid and successful biliary cannulation, hence lowering the risk of PEP [26].

Large papillary balloon dilation either after a small sphincterotomy or performed on a native papilla is a technique used in facilitating extraction of difficult bile duct stones. Recent studies suggested that prolonged dilation intervals of up to 5 minutes could both improve efficacy and decrease the risk of PEP associated with such procedure [27].

ERCP-associated infections. In 1987, Allen et al. [28] reported that duodenoscopes were responsible for patient-to-patient transmitted *Pseudomonas aeruginosa* infections, resulting in abscess formation and death [28]. Even though the use of ERCP and reprocessing standards including high level disinfection (HLD) have improved over the years, it was only after 2000 that more and more ERCP-associated infection outbreaks began to be reported worldwide, mostly in the

United States. The risk factors for ERCP-associated infections are biofilms (matrices of extracellular proteins produced by bacteria to protect themselves against antibiotics and disinfectants) production and the elevator mechanism at the distal tip of the endoscope, a hard-to-reach area for optimal physical cleaning and disinfecting [29, 30].

Beside the latest notifications for alternative reprocessing methods such as the use of non-thermal sterilization, finding innovative ways to prevent infections are considered: accessibility in the technological design of endoscopes, enhanced protocols for reprocessing surveillance, manufacturing disposable endoscope parts or even disposable endoscopes. Duodenoscopes with detachable distal end have now been developed, but it is not clear whether these will reduce the number of infections' transmission [31].

Finally, despite millions of gastrointestinal endoscopies performed annually, associated infections remain exceptionally rare (1%). This means either that we are dealing with a low risk of infection or that the real incidence is under-reported.

The future. Over the past half-century, there were considerable advances in the practice and performance of ERCP. An elegant personal review of fifty years of ERCP was recently published by Peter B. Cotton [32], a pioneer in the field, describing the history of this amazing revolution of ERCP, an endoscopic technique which has undoubtedly changed since its inception, but still remains and continues to be a safe and effective method for the treatment of pancreaticobiliary diseases [32]. Even more, new applications of ERCP have already occurred or are on the horizon: cholangioscopy and pancreatoscopy-guided lithotripsy of bile and pancreatic stones, treatment of benign bile tract strictures using fully covered metallic stents [33] or biodegradable biliary stents [34], ERCP-targeted bile duct application of radiofrequency ablation in the management of unresectable bile duct and pancreatic cancer [35]. Intraductal radiofrequency ablation of residual neoplasia after endoscopic papillectomy has proved a good and safe alternative to surgery [36]. Photodynamic therapy is an evolving application for the treatment of patients with unresectable hilar cholangiocarcinoma, which prolongs metal stent patency by comparison with biliary stent therapy alone [37].

ERCP represents a major advance in gastrointestinal endoscopy and adverse events, including infections, cannot diminish its critical importance. Recognizing the outstanding therapeutic role of ERCP in clinical practice with millions of procedures performed each year worldwide, to prohibit ERCP would seem impossible.

Finally, the future of ERCP depends also on the technological progress of noninvasive therapeutic procedures and the development of new medical or surgical therapies for pancreatic and biliary diseases.

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