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A modern approach to ERCP: maintaining efficacy while optimising safety

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Abbreviations:

PEP = Post-ERCP Pancreatitis

NKS = Needle-Knife-Sphincterotomy

ERCP = Endoscopic Retrograde Cholangio Pancreatography

CT = Computed Tomography

CT-IVC = Computed Tomography Intravenous Cholangiography

MRCP = Magnetic Resonance Cholangio Pancreatography

EUS = Endoscopic Ultrasound

PD = Pancreatic Duct

CBD = Common Bile Duct

RCT = Randomised Controlled Trial

ES = Endoscopic Sphincterotomy

EPLBD = Endoscopic Papillary Large Balloon Dilatation

SEMSc = Covered Self-Expanding Metal Stent

PS = Plastic Stent

CI = Confidence Interval

ABSTRACT

Background: ERCP is technically challenging and complications such as Post-ERCP pancreatitis (PEP) remain a concern. Modern ERCP techniques aim to maintain efficacy and improve safety. There are limited data regarding efficacy and safety of ERCP performed by a newly-qualified practitioner using modern techniques.

Aims: To conduct an ERCP practice audit and compare it with an Australian national survey. To review the evidence-base underlying modern ERCP practice.

Methods: All ERCPs performed by a newly-qualified practitioner, using prospectively collected data, from September 2011 to May 2015, were audited. Outcomes were compared to an Australia-wide survey of ERCP practice. A literature review was performed regarding recent developments in ERCP practice.

Results: The audit results correlated well with national data. All 478 ERCPs were therapeutic and had pre-procedure imaging. Wire-guided biliary cannulation was used. The success rate was 97%. The overall adverse-event rate was 0.8%. Choledocholithiasis was the predominant indication (72%). In 53 (16%) difficult biliary cannulations, the needle-knife-sphincterotomy (NKS) rate was low compared to national data (13% vs 33%). The rate of dual-wire cannulation technique was higher (87% vs 30%). Pancreatic duct stenting (performed in 32 cases (70% of dual-wire cannulation cases)) and rectal indomethacin (25%) were used to reduce PEP risk.

Conclusions: A newly-qualified ERCP proceduralist achieved high success rates with minimal adverse events, using modern techniques. Practice was consistent with national data, although dual-wire cannulation technique was preferred to NKS. The evidence-base for modern ERCP techniques was reviewed. ERCP efficacy and safety should be monitored by practice audit.

KEYWORDS

Cannulation

ERCP

Post-ERCP pancreatitis

INTRODUCTION

Diagnostic ERCP evolved rapidly after the first reported endoscopic cannulation of the Ampulla of Vater in 1968[1]. The era of therapeutic ERCP commenced in 1974 with the invention of endoscopic sphincterotomy[2]. Nonetheless, a significant proportion of ERCPs remained diagnostic. Adverse events associated with ERCP, and advances in non-invasive imaging modalities, have resulted in ERCPs being performed almost exclusively for therapeutic indications. While high rates of efficacy were expected from ERCPs over the last two decades, adverse-event rates remained high. Therefore, a significant focus of recent ERCP research and practice has been on improving its safety profile.

Commencing consultant practice following completion of ERCP training is a challenging period. It is important to audit personal practice and compare the results with broader data, to assess that efficacy and safety are adequate. Studies have shown benefits of modern techniques including pre-procedure imaging, wire-guided cannulation, dual-wire technique in difficult cannulations, prophylactic pancreatic duct (PD) stenting and rectal indomethacin. Recently, Ting et al described modern ERCP practice trends in Australia via a nation-wide survey[3]. However, there are limited data reporting success and adverse-event rates for newly-qualified ERCP proceduralists, using modern techniques.

The aims of this study were to assess the outcomes of a newly-qualified ERCP proceduralist (AM), compare it with the national survey data, and review the evidence-base underlying modern ERCP practice. Prior to commencing consultant practice, AM undertook 2 years of ERCP training at high-volume centres at Westmead hospital, Sydney, Australia and St Michael's Hospital, Toronto, Canada.

METHODS

All ERCPs performed by AM since commencing consultant practice, over a 3.75 year period from September 2011 – May 2015, were retrospectively analysed from prospectively collected data. Patients referred as inpatients underwent ERCP in an inpatient setting and outpatients underwent ERCP as a day-stay procedure. Data collected included: ERCP indications, pre-operative imaging, biliary cannulation technique and success rates, PEP prophylaxis methods, stent insertion (biliary or pancreatic) and adverse events. The outcomes were compared to practice trends, as reported in the recent Australia-wide web-based survey of ERCP practitioners[3]. This comprised forty questions that logically progressed.

109 of 227 registered ERCP practitioners around Australia completed the survey, providing a cross-sectional impression of practice trends. A literature review was then performed, to determine the evidence-base underlying contemporary ERCP practice.

RESULTS

Indications

478 ERCPs were performed by AM between Sept 2011 and May 2015. Indications were: 344 (72%) choledocholithiasis or cholangitis, 100 (21%) biliary strictures (including pancreas head carcinoma), 24 (5%) bile leaks, 6 (1%) biliary stent removals, 3 endoscopic ampullectomies and 1 sphincter of Oddi dysfunction. The indications were consistent with those in the national survey, where the commonest indications were choledocholithiasis, followed by malignant biliary obstruction and then bile leaks.

Pre-procedural imaging

All patients had pre-procedural imaging, including 169 (35%) CT or CT cholangiography, 141 (29%) MRCP, 97 (20%) ultrasound, 57 (12%) intra-operative cholangiogram and 19 (4%) Endoscopic Ultrasound (EUS).

Cannulation

All 478 patients had pre-procedure antibiotics as prophylaxis against cholangitis. Fourteen had luminal obstruction or stenosis, or surgically altered anatomy, and the major papilla could not be reached. Of the remaining 464 cases, 116 had previous ERCP and sphincterotomy that enabled biliary access. The remaining 348 (75%) had naïve papillae and successful biliary cannulation was achieved in 338 (97%). Wire-guided cannulation using a sphincterotome and 0.035" guidewire was the initial cannulation technique used in all cases. Standard wire-guided cannulation was successful in 285 patients (84%). The use of wire-guided cannulation was consistent with the current Australian trend, where 90% of respondents identified it as their preferred cannulation technique.

In the remaining 53 (16%) patients, where standard wire-guided cannulation was not achieved, 46 (87%) were successfully cannulated using the dual-wire technique. Seven cases (13%) required needle-knife-sphincterotomy. In comparison, for difficult cannulations, the frequency of NKS was significantly higher in the national survey (33%) and the frequency of dual-wire technique was significantly lower (30%).

Pancreatic duct (PD) stenting and rectal indomethacin for PEP prophylaxis

Of the 46 patients with biliary cannulation via the dual-wire technique, 32 (70%) had temporary PD (single pigtail) stents placed as prophylaxis against PEP. PD stenting was performed after a second

inadvertent PD cannulation. In the national survey, 77% of practitioners reported using PD stents for prophylaxis in high-risk cases.

A 100mg rectal indomethacin suppository was administered to 121 (25%) patients with increased risk of PEP. Proteolytic agents were not used for PEP prophylaxis. The national survey revealed that 61% of Australian practitioners utilise rectal indomethacin selectively and 17% administer it in all cases.

Adverse events

Four patients (0.8%) experienced an adverse event. This included 2 cases of mild pancreatitis, corresponding to a 0.6 % rate of PEP for naïve papillae. There were 2 cases of post-sphincterotomy bleeding that were managed endoscopically to achieve haemostasis. There were no cases of severe pancreatitis or perforations.

DISCUSSION

Pre-procedure imaging, wire-guided cannulation and prophylactic measures against PEP, enabled a newly-qualified consultant to achieve high biliary cannulation rates (97%) and low complication rates (0.8%). Results were comparable to national practice trends, with the exception of cases of difficult biliary cannulation, where dual-wire cannulation technique was preferred to NKS. With this approach, ERCP practice by a newly-qualified proceduralist was safe and effective. The evidence-base underlying modern ERCP techniques is discussed here.

Pre-procedure imaging

For the diagnosis of choledocholithiasis, which is the most common indication for ERCP, conventional ultrasound and spiral CT demonstrate a sensitivity of 75-80%[4]. In comparison, MRCP, CT-IVC and EUS offer higher diagnostic accuracies.

A prospective Australian study of 65 non-jaundiced patients, comparing the accuracy of CT-IVC with ERCP, demonstrated a sensitivity of 95.6% and specificity of 94.3% with CT-IVC[4]. While ERCP was indeterminate in 4.7% of cases because of failed biliary cannulation, CT-IVC was indeterminate in 6.3% of cases because of inadequate duct opacification. Therefore, the rates of successful diagnosis were comparable.

MRCP is advantageous in jaundiced patients, as CT-IVC often fails to demonstrate bile duct opacification when serum bilirubin is greater than 2-3 times the upper limit of normal. A meta-analysis of 13 studies that compared MRCP to ERCP, demonstrated a mean sensitivity of 93% and specificity of 94% for

choledocholithiasis with MRCP. However, sensitivities in conditions such as malignancy were lower, ranging from 81% to 94%[5].

EUS is more labour-intensive, requires intra-venous sedation, a specially-trained endoscopist and is minimally invasive. Consequently, it is less readily available than CT-IVC or MRCP. It achieves comparable diagnostic accuracy to MRCP, though this is operator-dependent. An advantage of EUS performed prior to ERCP is that EUS may be performed in the same session, with ERCP immediately following, where the EUS is positive. A meta-analysis that included 2673 patients with suspected choledocholithiasis in 27 studies showed that EUS had a pooled sensitivity of 0.94 (95%CI, 0.93-0.96) and a specificity of 0.95 (95%CI, 0.94-0.96)[6]. A prospective randomised study compared the outcome of EUS followed by ERCP (33 patients) vs ERCP alone (32 patients). The rate of diagnosis of choledocholithiasis was similar in both groups, though complications were significantly higher in the ERCP only group[7].

Therefore, pre-ERCP imaging techniques allow for selection of appropriate patients on whom to perform therapeutic ERCP, and reduce unnecessary procedures and their associated adverse events.

Wire-Guided vs Contrast-guided Cannulation

Biliary cannulation is performed using a catheter or sphincterotome device, using either a guidewire or by injecting contrast, under fluoroscopic guidance, through the papilla. Contrast-guided cannulation may result in inadvertent injection of contrast into the PD. This is an independent risk factor for PEP.

Multiple studies have compared the efficacy and safety of these techniques, with conflicting results. A prospective non-randomised comparative-intervention study involving 1258 ERCPs, showed that CBD cannulation success rates were similar in wire-guided (83.7%) and contrast-guided (85.5%) techniques[8]. There were no statistically significant differences in the PEP rate in both groups (5.2% vs 4.4%, p=0.60)[8]. However, an Australian RCT comparing wire-guided and contrast-guided techniques demonstrated cannulation success rates of 81.3% (wire-guided) vs 73.9% (contrast); p=0.03[9]. A meta-analysis of 7 RCTs demonstrated pooled cannulation success rate of 89% (guidewire) vs 78% (contrast); RR:1.19; [95%CI: 1.05-1.35][10]. The PEP rate was 3.2% (guidewire) vs 8.7% (contrast); RR:0.38; [95%CI: 0.19-0.76]. Subgroup analysis showed a significantly lower PEP rate after guidewire entry versus contrast injection of the PD (1.1% vs 9.5%; RR:0.19; [95%CI, 0.06-0.58])[10].

Therefore, wire-guided cannulation has become the pre-eminent technique in Australia. However, contrast-guided cannulation remains an alternative, particularly as studies that do not demonstrate superiority for wire-guided cannulation, continue to be published[11].

Needle-Knife-Sphincterotomy (NKS)

Needle-Knife-Sphincterotomy is generally used when standard biliary cannulation fails. NKS involves direct incision into the CBD using electrocautery via a needle-knife, without wire guidance. In an Australian RCT of 464 patients undergoing consecutive ERCPs, 73 were identified as being difficult biliary cannulations according to pre-defined criteria. They were randomised to early NKS or persisting with standard cannulation technique. While the overall cannulation success rate in these 73 patients was 86%, 65% of the standard technique arm had to crossover to the NKS arm. This demonstrated that NKS is effective in cases of difficult biliary cannulation, where standard techniques fail[12].

However, NKS is a major risk factor for PEP and multivariate analyses have demonstrated this, even after adjusting for other confounding factors[13]. A prospective multicentre Chinese study of 3178 ERCPs performed on 2691 patients demonstrated that NKS had the highest odds ratio for development of post-ERCP adverse events (OR:2.70, 95%CI: 1.42–5.14, P=0.002), including PEP (OR:4.34, 95%CI: 1.92–9.79, P<0.001) and asymptomatic hyperamylasaemia (OR:2.34, 95%CI: 1.32–4.14, P=0.004)[14].

Reducing NKS use vs reducing multiple standard cannulation attempts

Some studies suggest that NKS does not independently affect the PEP rate, and that this is related to multiple cannulation attempts and resultant papillary oedema that usually precede NKS[15-17]. A retrospective study of 2004 ERCPs showed that pancreatitis occurred in 2.7% of patients who underwent biliary cannulation without NKS and in 6.5% with NKS (p=0.006). However, the PEP rate was lower when NKS was performed before 10 standard cannulation attempts were reached, when compared with greater than 10 standard cannulation attempts without NKS[15].

Swan et al found that in difficult biliary cannulations, there was no significant difference in PEP rates among patients in the early NKS group compared with persisting standard cannulation technique (20.5% vs 17.6%). However, more than 7 cannulation attempts increased the risk of PEP (p<0.01)[12]. They concluded that early initiation of NKS was not associated with PEP. However, failure of early cannulation, with resulting multiple cannulation attempts, was a significant risk factor. This conclusion was supported by another Australian RCT involving 414 patients, which showed that the PEP risk increased incrementally with each attempt at the papilla (OR:1.4 per attempt, P=0.04), to greater than 10 % after four or more attempts[9].

It is our view that practitioners should recognise their strengths and limitations with respect to both NKS and standard cannulation, and apply the strategy most likely to result in prompt cannulation with the least risk to patient safety.

Dual-guidewire technique in difficult biliary cannulation

Pancreatic guidewire placement has been shown to be useful in difficult biliary cannulations, by straightening the common channel and enhancing biliary cannulation with a second guidewire. Therefore, when the PD is inadvertently cannulated with a guidewire, rather than withdrawing the wire, it is temporarily left within the PD. A second guidewire is passed alongside the existing wire and manipulated into the CBD. Prior to PD wire removal, PD stent placement should be considered for prophylaxis against PEP.

In a retrospective study, the dual-guidewire technique was successful in 72% of difficult biliary cannulation cases, where single-guidewire cannulation failed, whereas pre-cut sphincterotomy had a 46% success rate[18]. The incidence of PEP was 8% for single-guidewire technique, 4% for dual-guidewire technique and 0% for pre-cut sphincterotomy[18].

Therefore, dual-guidewire technique may become the preferred salvage technique, rather than NKS, when single-guidewire cannulation is unsuccessful. We have adopted this approach, however, the Australian survey data indicated equal usage of these techniques (30% dual guidewire vs 33% NKS) as the second-line option[3]. Prospective randomised studies will be required to better determine the optimal second-line cannulation technique.

Prophylactic Pancreatic Duct (PD) stenting

Prophylactic PD stenting has been shown in several RCTs to be effective in reducing the PEP rate, by facilitating drainage of the PD. A meta-analysis involving 8 RCTs and 10 non-randomised trials showed that PD stenting significantly reduced the risk of PEP (OR:0.22, 95%CI 0.12-0.38; p<0.01). The absolute risk difference was 13.3% (95%CI, 8.8%-17.8%), with a number needed to treat of 8 (95%CI, 6-11)[19].

However, there are risks associated with using PD stenting as a routine prophylactic technique. Even in expert centres, the failure rate of PD stenting ranges from 5-10%, particularly when there is unfavourable PD anatomy[13]. Furthermore, PD cannulation is itself a risk factor for PEP. In a prospective study of 800 consecutive ERCPs by Nakai et al, analysing risk factors for PEP in wire-guided cannulation, CBD diameter <9mm (OR:2.03, p<0.006) and unintentional guidewire insertion into the PD (OR:2.25, p<0.014) were the only statistically significant risk factors for PEP. The PEP rate also incremented with the number of PD wire passes (zero PD wire passes vs >10 PD wire passes: 5.3% vs 18.9%)[20]. Therefore, our practice is to avoid deliberate PD cannulation. We reserve PD stenting for repeated inadvertent PD

cannulations, with a lower threshold for stent placement in high-risk cases. The exception to this rule is endoscopic ampullectomy, where we deliberately cannulate the PD following ampullectomy, to facilitate PD stenting. This is due to the known high risk of PEP following endoscopic ampullectomy, in the absence of PD stenting.

Current European guidelines to prevent PEP recommend PD stenting in higher risk procedures such as pre-cut sphincterotomy and with repeated inadvertent PD cannulations[21].

Endoscopic papillary large balloon dilatation (EPLBD)

While endoscopic sphincterotomy (ES) is the standard method of enlarging the papillary orifice before stone retrieval, EPLBD following sphincterotomy, is a newer technique that may reduce the need for mechanical lithotripsy and improve clearance of larger stones.
In a randomised trial of 156 consecutive patients comparing EPLBD after ES to ES alone, there was no significant difference in the clearance rate of stones (ES vs EPLBD: 88.5% vs 89%). However, more mechanical lithotripsy was required in the ES only group (46.2% vs 28.8%, p=0.028). For stones >15mm, this difference was further accentuated (90.9% vs 58.1%, p=0.002). There was a trend towards reduced morbidity in the EPLBD group (ES vs EPLBD: 10.3% vs 6.8% p=0.46). The cost of hospitalisation was significantly lower in the EPLBD group (US$6005 vs US$5025, p=0.034)[22].

In our experience, EPLBD is also useful in cases of difficult papillary access, or where the papilla is within or on the margin of a large diverticulum. In such cases, where a complete sphincterotomy may risk causing a perforation, we perform a partial sphincterotomy to the maximum safe point and then use balloon dilatation to complete the disruption of the papillary sphincter. In Australia, EPBLD is routinely performed by up to 54% of endoscopists for extraction of large CBD stones[3].

Covered self-expanding metal stents (SEMSc) vs plastic stents (PS)

Traditionally, ERCP proceduralists have used either uncovered self-expanding metal stents or plastic stents for the treatment of biliary strictures. Metal stents were placed for inoperable malignant strictures and PS were placed for operable malignant biliary strictures or for benign strictures. However, the development of SEMSc is changing ERCP practice. A SEMSc is significantly more expensive than a single PS. However, recent studies have demonstrated that the use of SEMSc rather than PS, has both clinical and economic advantages. A European RCT of 63 patients with operable malignant biliary obstruction, requiring biliary stenting prior to surgery, were randomised to receive either SEMSc or PS[23]. The pre-operative complication rate in the SEMSc group was significantly lower (SEMSc vs PS: 8.6% vs 35.7% p=0.012). The mean hospitalisation duration was also significantly lower in the SEMSc group

(SEMSc vs PS: 0.2 ± 1 day vs 2.7 ± 4.7 days; p=0.011). This was due to a trend towards additional interventions including repeat ERCPs and hospital re-admissions in the PS group compared to the SEMSc group (PS vs SEMSc: 8.6% vs 25%), though this was not statistically significant (p=0.077). Hence, while SEMSc are more expensive, the overall costs incurred in the SEMSc group were lower (SEMSc vs PS: € 1486 ±129 vs 2117 ± 643; p=0.34)[23].

In an American RCT involving 113 stents in 52 patients with pancreatic cancer, the incidence of complications such as stent occlusion, cholangitis and stent migration were 7 times higher in the PS group (PS vs Metal: 0.20 vs 0.03 p<0.05)[24].

SEMSc have the advantage of being removable, and are increasingly recognised as being effective for management of benign biliary strictures[19].

EUS-guided biliary access

A novel strategy in failed biliary cannulations, is the use of EUS to access the CBD. Trainees are increasingly being trained in both ERCP and EUS, with survey data indicating that 25% of Australian ERCP practitioners had formal EUS training[3]. Although EUS-guided biliary access is tempting, it should not replace good ERCP technique as risks associated with EUS-guided access can be high. In a prospective study of EUS-guided biliary drainage performed following 38 failed ERCPs from 2514 consecutive ERCPs, the success rate was 79%. However, 7 patients (18%) suffered adverse events ranging from mild bile leaks to pseudocyst formation[25]. In most tertiary Australian centres, the annual case volume of unsuccessful biliary cannulations is low, possibly precluding proficiency in the EUS-guided technique. A recent prospective cohort study in an expert ERCP centre showed that EUS-guided biliary drainage was required in only 3 out of 524 ERCPs (0.6%)[26]. Therefore, careful consideration must be given to whether pursuing this technique is appropriate, particularly with the high success rates of alternative techniques like percutaneous trans-hepatic cholangiography (PTC).

Reducing PEP by rectal indomethacin and aggressive intra-venous fluids

A multi-centre RCT examined the impact of rectal indomethacin, administered immediately after ERCP, on the incidence of PEP, in high-risk patients. Out of 602 patients, PEP occurred in 16.9% in the placebo group and 9.2% in the rectal indomethacin group (p=0.005)[27]. Rectal indomethacin is also useful in reducing PEP in the setting of failed PD stent placements. A secondary analysis of RCT data showed that the PEP rate following failed PD stent placement was significantly higher when compared with successful PD stenting (34.7% vs 16.4%)[28]. However, when this regression analysis was repeated in the rectal indomethacin sub-group, failed PD stent placement was not significantly associated with PEP[28].

A recent RCT compared a pre-specified regimen of aggressive intra-venous hydration during and following ERCP, with standard hydration. 39 patients were randomised to the aggressive hydration arm and 23 to standard hydration arm. There was a significant protective effect of aggressive hydration in relation to the development of PEP (0% vs 17 %, p=0.012), with no cases of volume overload[29].

Referral to a high-volume centre

Finally, referral to a high-volume centre following unsuccessful ERCP is effective. An Australian study demonstrated high success rates, with a favourable adverse-event rate compared to routine ERCPs[30]. In this prospective intention-to-treat analysis of 51 patients referred following recent unsuccessful ERCP, successful biliary cannulation was achieved in 100% of cases. Adverse events including PEP occurred in 3.9%. An identifiable cause for the previous unsuccessful cannulation, such as altered anatomy, was found in 55% of cases.

CONCLUSIONS

ERCP has evolved significantly since its origins. While high rates of efficacy have been achieved, further progress in achieving safer outcomes is required. The transition from being a trainee endoscopist to an independent consultant is challenging, however we have showed that a newly-qualified Australian ERCP proceduralist achieved high success rates with a very low adverse-event rate, by using modern, evidence- based techniques. Practice was consistent with Australia-wide trends, except that dual-wire cannulation technique was preferred to NKS for difficult cases. The efficacy and safety resulting from modern ERCP techniques should be monitored by practice audit as a quality assurance measure.

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CONFLICT OF INTERESTS

Authors declare no conflict of interests for this article.

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