from the problems of cross-sectional design. A further development of the aetiological research of GORD would therefore be to assess incident cases of GORD. Such research would supply us with a reliable estimation of the incidence of GORD and also increase the validity of the aetiological research of GORD.

Gut 2007;**56**:741–742.

doi: 10.1136/gut.2006.112243

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Competing interests: None declared.

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Sphincter of Oddi dysfunction

Prospective comparison of secretin-stimulated MRCP with manometry in the diagnosis of sphincter of Oddi dysfunction types II and III

John Baillie, James Kimberly

Is the role of secretin in causing a choleresis clinically significant enough to be a “stress test” for biliary SOD?

Every specialty in Medicine has its orphan diagnosis; in ophthalmology it's “dry eyes”, in gynaecology “dyspareunia”, in rheumatology “fibromyalgia” and the list goes on. In gastroenterology, the vast diagnostic and therapeutic wasteland is irritable bowel syndrome (IBS). However, deep within IBS (or more correctly, chronic functional abdominal pain syndrome) there is an almost impenetrable jungle, called sphincter of Oddi Dysfunction (SOD). It is not a place for the faint-hearted. SOD as a fashionable diagnosis first appeared on the radar screen in a 1989 *N Engl J Med* paper: a group of US investigators published their experience of endoscopic (biliary) sphincterotomy (EBS) in patients with postcholecystectomy pain.¹ The authors divided SOD into three categories depending on the presence or absence of transiently abnormal liver serologies and/or common bile duct (CBD) dilatation. “Typical” biliary-type pain was needed to make the SOD diagnosis. Type I patients had “typical” biliary pain, transient serum transaminase elevations to at least 1.5 times the

upper limit of normal with normalisation between attacks on ≥ 2 occasions, and a CBD ≥ 12 mm in diameter. Type II patients had pain and enzyme elevations or a dilated CBD, but not both. Type III patients had a pain syndrome alone. (The original classification included delayed drainage of contrast from the bile duct after ERCP as an addition criterion. Most investigators have dropped this from the classification, as it has been shown to be unreliable). The so-called Milwaukee Classification of SOD has survived unchanged for 17 years, despite growing evidence that it is flawed and in need of revision.² This is not intended as a criticism of the original investigators, who tried their best to make sense of a difficult pain syndrome in a demanding group of patients. Under the recently promulgated Rome III Criteria,³ SOD is now part of a biliary dyskinesia syndrome that includes gallbladder dysmotility in those who have not had that organ surgically removed. Most ERCP endoscopists who see cases of postcholecystectomy pain feel that type I SOD should be dropped from the classification. It is not a

motility disturbance but a mechanical (papillary) stenosis of the biliary outlet. It is effectively treated by EBS, with $>95\%$ long-term “cure” rates.⁴ Indeed, this outcome is so predictable that we do not bother to perform sphincter of Oddi manometry (SOM) in the patients: the result is the same regardless of the sphincter pressure measured. SOM is a technically demanding technique used to measure biliary and pancreatic sphincter pressures. Typically, SOM is limited to large referral centres, which can justify the investment in expensive equipment to help evaluate patients with postcholecystectomy pain syndromes and idiopathic pancreatitis.⁵ On the heels of biliary SOD came an inevitable attempt to similarly classify pancreatic sphincter dysfunction.⁶ A useful discussion of pancreatic SOD is beyond the scope of this commentary, but it will suffice to say that it is imperfect and even more confusing to many of us than biliary SOD! Unfortunately, SOM has developed a bad reputation for causing post-ERCP pancreatitis, especially in patients with type III SOD.⁷ As Freeman *et al*⁸ have pointed out however, the act of performing pressure measurement is not the problem, the risk comes from instrumenting a normal or hypersensitive duodenal papilla and perfusing a catheter within the confines of a small-calibre (ie, normal) pancreatic duct. Efforts have been made to reduce this risk using catheters with simultaneous aspiration during perfusion, with reported benefit in the hands of enthusiasts.⁹ Post-ERCP pancreatitis (PEP) rates of 15–20% after SOM are not uncommon,¹⁰ although routine stenting of the pancreatic duct after manometry (with or without sphincterotomy) is probably lowering these numbers.

The term “Holy Grail” is much abused these days, but if you define it as a much-desired object or goal that transforms

lives, then a non-invasive test for SOD type II and III is surely the Holy Grail of the ERCP world. In this issue of *GUT*, a group of British investigators report the results of an interesting study using secretin-stimulated magnetic resonance cholangiopancreatography (ss-MRCP) to predict the presence of type II and III SOD and the outcome of EBS (see page 809).¹¹ MRCP has come a long way in the last 5 years, largely replacing diagnostic ERCP in many clinical situations. As indicated by the authors, MRCP is non-invasive, does not require sedation, and permits accurate assessment of parenchymal and ductal abnormalities in the pancreas and biliary tree.¹² The study included patients who were >18 years of age, who had recurrent pancreatic and/or biliary type pain unresponsive to medical therapy for at least 6 months requiring hospitalisation and/or narcotic analgesia, or idiopathic pancreatitis with negative cross-sectional imaging and standard upper gastrointestinal endoscopy (oesophago-gastroduodenoscopy). Patients with possible mechanical causes for their symptoms (eg, gallstones, ampullary tumours), current alcohol abuse and pregnant women were also excluded. SOM was performed in the standard fashion.¹³ An abnormal ss-MRCP was defined as a >1 mm increase in pancreatic duct diameter 3 min after intravenous injection of 1 IU/kg of a synthetic form of the hormone, secretin and/or ductal dilatation persisting >7 min after secretin injection. Although the authors cite that these findings are "suggestive" of SOD, their only reference is to a Belgian study published in the radiology literature.¹⁴ We don't believe there is any consensus at present in the ERCP endoscopy community on the relationship of ss-MRCP findings to SOD.

The primary end point of the study was a comparison of ss-MRCP with SOM for the diagnosis of type II and type III SOD. Secondary end points were evaluation of the risk of post-ERCP pancreatitis in patients with suspected SOD with or without EBS and assessment of outcome after investigation with or without endoscopic treatment. A total of 47 patients (9 men, 38 women) with a mean age of 46 years were recruited into the study; 7 were subsequently excluded with a diagnosis of chronic pancreatitis. ss-MRCP was abnormal in 10 of 16 (63%) type II patients but in none of the 11 patients with type III SOD. 14 of 16 (87%) type II patients, but only 2 of 11 (18%) type III patients had significant improvement in pain score after endotherapy (EBS). The sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy of ss-MRCP in the setting were reported to be

37%, 85%, 83%, 39% and 52%, respectively. 9 of 13 (69%) patients with normal SOM reported that their symptoms improved without EBS over a follow-up period of 17–44 months (mean 28 months). Only 2 of 11 patients with manometrically proven type III SOD reported improvement after a mean follow-up of 30 months. Thus, patients with type II SOD and abnormal SOM were more likely to benefit from EBS than manometrically abnormal type III patients. All 12 patients with SOD who had an abnormal ss-MRCP reported long-term improvement after EBS. In all, 5 (10.6%) patients developed post-ERCP pancreatitis (PEP), 4 mild and one moderate; 4 of the 5 were patients with type III SOD. None of the patients who had SOM without EBS developed PEP. The authors conclude that "ss-MRCP is insensitive in predicting abnormal (sphincter of Oddi) manometry in patients with suspected Type III SOD, but is useful in selecting out patients with suspected SOD Type II who are most likely to benefit from endotherapy". Regarding the secondary end points of the study, the risk of PEP was reportedly significantly higher in patients with SOD type III compared with those with normal SOM ($p = 0.031$), and there was "a trend towards an increased risk of [PEP] in patients with SOD Type III as compared to SOD Type II" ($p = 0.125$). Patients with type III SOD had a generally poor symptomatic response to EBS compared with those with type II. Patients with an abnormal ss-MRCP, were diagnosed with type II SOD in 83% of cases, did significantly better over time than those with normal ss-MRCP.

The investigators are to be congratulated on tackling a notoriously difficult problem (SOD) in a prospective study of this kind. In the US, patients with SOD represent a very mobile population which is difficult to track over time. Longitudinal data (in this study extending >3 years) are rare in the SOD world, and most welcome. This is a very "busy" paper. We found it difficult here and there to separate the wood from the trees. Our first impression on reviewing the data was that the study was likely underpowered. After exclusions following ERCP and ss-MRCP, the "n" was quite small: patients with bona fide SOD are hard to find. When evaluating sensitivity, specificity, positive and negative predictive values, and accuracy, 95% CIs are necessary to interpret the results. These were absent from the paper, so we calculated them for ss-MRCP: sensitivity 37% (95% CI 21% to 56%), specificity 85% (95% CI 57% to 97%), PPV 83% (95% CI 54% to 97%), NPV 39% (95% CI 20% to 63%). The 95% CI for the PPV of ss-MRCP (54% to 97%) suggests that it is little better than a coin toss. In our opinion, this study lacks the

statistical "clout" to justify abandoning SOM in favour of ss-MRCP as first-line evaluation for SOD type II. Hopefully, future (likely multicentre) studies will answer that question for us. Is the role of secretin in causing a choleresis clinically significant enough to be a "stress test" for biliary SOD? Again, this would be a fertile area for study. The fate of patients worked up for presumed SOD type III but who do not undergo EBS remains uncertain. This study suggests that most type III patients fail to benefit from endoscopic biliary sphincterotomy (EBS) even when SOD pressures are elevated. The old adage that "no one ever died of Type III SOD" is probably true. Does the "biliary pain" go away with time? Nine out of 13 patients with suspected Type III SOD but normal manometry in this study spontaneously improved over a mean follow-up of 28 months. This is a very important—and possibly unique—observation. The authors mention intrapapillary botulinum toxin (BoTox) as a possible treatment for SOD¹⁵ in their Discussion. The jury is still out on BoTox in this setting, and in our opinion its use should be confined to clinical trials. It would be interesting to perform ss-MRCP before and after BoTox injection in manometrically proven SOD to assess its effect. Finally, we should not forget that fancy tests are expensive, and that ss-MRCP is no exception. In the US, third party payers (insurers) will have to be convinced that it is cost-effective to spend \$3000 or more on the diagnosis of suspected SOD. In some centres—including our own—patients are required to pay for the secretin injection, which is not covered by insurance. A sum of \$350 is too "rich" for many, and the alternative—a non-secretin stimulated MRCP—is a lost opportunity to assess both structure and function of the pancreas.^{16, 17} Future studies should assess the optimal dosage of secretin for ss-MRCP, in the hope of keeping cost down without sacrificing quality.

Gut 2007;56:742–744.

doi: 10.1136/gut.2006.111278

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Competing interests: None.

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Endoscopic practice

Are we meeting the standards set for ERCP?

John Baillie, Pier-Alberto Testoni

ERCP practice today: implications for training

The study by Williams *et al.*,¹ published in this issue of *Gut* (see page 796), reports the findings of a UK National Confidential Enquiry into Patient Outcomes and Deaths relating to endoscopic retrograde cholangiopancreatography (ERCP). Approximately 48 000 ERCPs are performed annually in the UK. For this study, five metropolitan areas of England were surveyed. The authors estimate that about 20% of all the ERCP procedures performed in adults (>18 years of age) over a 6-month period were captured. The results offer a cornucopia of food for thought. In all, 94% (76/81) of endoscopy units polled responded. Personal questionnaires were returned by 89% of staff endoscopists and by 81% of their trainees. Aspects of ERCP that were examined ranged from the experience and success of the physicians performing the procedures, to indications, informed consent, adequacy of monitoring and resuscitation, and outcomes, including complications and mortality. More than a few of the findings are sobering, concerning and demand remedial action. But we acknowledge that it is easy to be an armchair critic of another country's ERCP practice. An in-depth look at ERCP practice in the US and Italy, for example, would probably reveal some, if not many,

of the same problems arising from marginal training, inexperience, inadequate volume of cases to maintain skills and so on.

The current study looked at the success rates of trainees as a function of their experience. Those with experience of >200 ERCPs had an unsupervised cannulation rate (to enter the duct of choice) of 66%; this fell to 40% for those with experience of <200 ERCPs. The overall trainee cannulation success rate with procedures whose trainee involvement was not documented, was reportedly 54%. The American Society for Gastrointestinal Endoscopy (ASGE) considers a selective cannulation success rate of 80% to be the bare minimum for credentialling to perform ERCP²; in the UK, the Joint Advisory Group on Gastrointestinal Endoscopy suggests that trainees aspire to a success rate of 90%.³ Until the 1996 publication of a large prospective study of ERCP training from the Duke University Medical Center,⁴ in which JB participated, ridiculously low numbers of procedures (eg, 25) were regularly touted as being adequate for credentialling to perform ERCP in the US. These numbers were usually suggested by gastroenterology training programme directors from hospitals with low ERCP

volumes. Keeping the credentialling threshold low was the only way to ensure that most or all their trainees could leave at the end of fellowship with a letter stating that they were "trained in ERCP". The Duke University study showed that to attain minimum competence (80% success rate) in a variety of diagnostic and therapeutic ERCP skills, not less than 180–200 cases were required. Recognising that there is no "magic" number of ERCPs that guarantees competence, the ASGE has taken the stance that a trainee will rarely be ready for credentialling to perform unsupervised ERCP with fewer than these numbers. Indeed, some trainees are still struggling after 300 or more procedures. The decision to let a trainee "loose" to do ERCP on his or her own is inevitably quite subjective. But those of us who train endoscopists and write letters of support for them to get hospital credentials take this duty seriously. The Australians have set the highest "bar" for credentialling—namely, 200 unassisted ERCPs (<http://conjoint.gesa.org.au/information.htm>). Other countries have compromised by taking the "middle ground"—for example, requiring 150 procedures. The present study is further evidence—if any was needed—that 200 ERCPs performed under supervision are insufficient to achieve a credentialling threshold of 80% success at selective cannulation. A total of 77% of trainers reported a successful selective cannulation rate of >80%. This means that almost a quarter (23%) of the trainers failed to achieve the ASGE threshold for competence in diagnostic ERCP. The overall completion of intended treatment was only 70% (62%, if the aim was to clear the bile duct of stones). In all, 81% of pancreatograms were reportedly "unintentional": this suggests difficulty in achieving selective cannulation of the