

Selected Summaries

Diagnostic approach to choledocholithiasis

Dwerryhouse SJ, Brown E, Vipond MN. (Departments of Surgery and Radiology, Gloucestershire Royal Hospital, Gloucester, United Kingdom.) Prospective evaluation of magnetic resonance cholangiography to detect common bile duct stones before laparoscopic cholecystectomy. *Br J Surg* 1998;**85**:1364–6.

SUMMARY

Over a two-year period, 40 cases of cholelithiasis with risk factors for common bile duct (CBD) stones (abnormal liver function test results, previous gallstone pancreatitis, dilated CBD of 7 mm or more, history of jaundice) underwent magnetic resonance cholangiography (MRC) scan. It could not be done in 2 cases due to claustrophobia; they underwent endoscopic retrograde cholangiography (ERC) and 1 was found to have a bile duct stone. After MRC, all patients underwent ERC and stones detected at ERC were cleared endoscopically. If ERC was unsuccessful, peroperative cholangiography was performed. At the end of the study, the MRC results were compared with the ERC and peroperative cholangiography findings. MRC identified CBD stones in 7 of the 8 patients with this condition. Two patients were misdiagnosed as having CBD stones by MRC. Thus, MRC had a sensitivity of 88%, positive predictive value of 78%, specificity of 93% and negative predictive value of 97%. If ERC had been limited to patients with positive or failed MRC, it would have been required in 11 patients instead of 40.

COMMENT

The diagnosis of CBD stones in patients undergoing cholecystectomy has long been a priority for surgeons. Although some stones can pass uneventfully, there is a 25%–50% risk of ductal stones giving rise to complications, some of which can be life-threatening.¹ Laparoscopic cholecystectomy is considered the gold standard by many surgeons, and thus it is even more important that adequate preoperative evaluation of the CBD is done, especially in those with a suspicion of CBD stones.

In patients with a high risk of CBD stones (based on history, ultrasound, biochemistry), the incidence of negative ERC is as high as 60%–70%.^{2,3} In a retrospective analysis of 1000 patients undergoing laparoscopic cholecystectomy, it was found that only 34% with a high suspicion of CBD stones actually harboured them.³ ERC is an invasive investigation and has a risk of post-procedural pancreatitis and sepsis if contrast is injected into a dilated system without clearing it subsequently, while sphincterotomy followed by stone extraction has a complication rate of around 10% and a mortality rate of around 1% in most series.⁴ The overall success rate of endoscopic clearance in most large series is approximately 90%. A few of these cases require more than one procedure along with adjuvant techniques of mechanical and laser lithotripsy. However, the success rates in routine community practice are much lower.⁴

One way of avoiding the potential morbidity of ERC is by separating the diagnostic and therapeutic arms of the protocol and restricting its use in only those patients with documented CBD stones. The availability of endoscopic and laparoscopic ultra-

sound and MRCP has made this possible with a degree of certainty that is not available with conventional ultrasound.

In a prospective comparative study of endoscopic ultrasound and ERCP in patients with suspected CBD stones, endoscopic ultrasound was slightly more sensitive than ERCP (93% v. 89%) although less specific (97% v. 100%).^{3,5} Endoscopic ultrasound has the advantage of being less invasive with no procedural complications. An important limitation is the very steep learning curve and the cost of the equipment.^{3,5}

Intraoperative tools for detection of CBD stones include the time-tested cholangiography and intraoperative ultrasound. Laparoscopic cholangiography has a failure rate ranging from 6% to 23%, depending on whether it is practised routinely or done on a selective basis.² False-positive rates are 3%–10%, which may result in unnecessary CBD exploration.⁶

Alternatively, laparoscopic ultrasound (like intraoperative ultrasound) has been used for the diagnosis of CBD stones. In a prospective, controlled, comparative study it was found that laparoscopic sonography was much more sensitive (100%) than laparoscopic cholangiography (75%) and was almost as specific as cholangiography (98% v. 99%). It was much faster than cholangiography (average procedural time 5.4 minutes v. 16.4 minutes) and was possible in all patients (100% v. 93%). This approach is, however, plagued with the same limitations as endoscopic ultrasound—cost and expertise.⁷

Laparoscopic cholecystectomy, laparoscopic cholangiography followed by postoperative ERC and stone extraction in patients with CBD stones is theoretically very attractive as only those with CBD stones are subjected to ERC. However, should endoscopic retrieval fail following laparoscopic cholecystectomy, the patient may have to be subjected to an open CBD exploration, making it a total of three procedures with the resultant morbidity and mortality being much more than that of open cholecystectomy with CBD exploration. In a recently published randomized trial, laparoscopic CBD exploration was comparable to postoperative ERC following laparoscopic cholecystectomy. While CBD clearance following the primary procedure was 75% in each group, eventually all patients in the laparoscopic CBD exploration group and 93% in the ERC group cleared following repeat ERCs, with no statistically significant difference in morbidity.⁸

MRC is a relatively new entry to the gamut of hepatobiliary imaging. In 1991, Wallner for the first time reported MRC using 2-dimensional breath-holding gradient echo sequences to image the biliary tract. On a heavily T2-weighted image, stationary fluid such as bile exhibits a high signal intensity, whereas the signal of the surrounding tissue is markedly suppressed. Technical refinements have resulted in decreased sensitivity to motion and respiratory artefacts, improved spatial resolution and decreased magnetic susceptibility and effects from bowel gas and metallic clips to negligible levels. As a result, the sensitivity of magnetic resonance in detecting intraductal abnormalities has improved from 81% to 100% in many recent series^{9,10} and stones as small as 2 mm in a dilated duct and 3 mm in a non-dilated system can be detected.^{9,10} The only caveat is the unlikely but possible event of confusing a stone for another type of intraluminal filling defect which can happen with a polyp, clot, parasite or pneumobilia, all of which result in false-positive reports.¹¹

The advantages of MRC are that it is non-invasive, does not require any contrast agents (hence there is no risk of dye sensitivity) and does not involve ionizing radiation. Imaging of the pancreatic duct is obtained at the same time along with excellent cross-sectional images and visualization of the liver and pancreas.^{10,11}

The major disadvantage of MRC is that it is a purely diagnostic technique unlike ERC which is both diagnostic and therapeutic. Nevertheless, the high negative predictive value of MRC may obviate the need for ERCP. The major advantage of MRC in the setting of suspected CBD stones may be not in detection of stones but in their exclusion; thus limiting the use of ERC to that of a therapeutic modality.^{10,11}

Although current reports have shown that with the new refinements MRC is comparable to ERC, factors of accessibility and cost-effectiveness are more important and would determine the status of routine MRC. The exact role of MRC in the diagnostic work-up of patients with suspected CBD stones requires further evaluation by means of prospective cost-effective outcome studies. Although one cannot escape the suspicion that the role of ERC in this setting has witnessed its zenith and will decrease in the future; as of now, preoperative ERC before laparoscopic cholecystectomy in the evaluation of suspected CBD stones continues to rule the roost.

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Should meta-analysis replace large randomized control trials?

Le Lorier J, Gregoire G, Benhaddad A, Lapierre J, Derderian F. (Research Center, Hotel-Dieu de Montreal Hospital, Department of Medicine, University of Montreal, QC, Canada.) Discrepancies between meta-analyses and subsequent large randomized, controlled trials. *N Engl J Med* 1997;337:536-42.

SUMMARY

This paper compared the results of systematically compiled large (defined as those which studied one thousand or more subjects), randomized, controlled trials with those of the relevant analyses published previously. The trials reported in the issues of *New England Journal of Medicine*, *The Lancet*, *Annals of Internal Medicine*, and the *Journal of American Medical Association*, from 1 January 1991 to 31 December 1994, were assessed for adequacy of sample size. Meta-analysis of similar topics that had been published before the corresponding trial were searched. The search strategy included use of MEDLINE without language restrictions, and references listed in the published trials. Those meta-analyses which were similar to the trial in terms of population studied, therapeutic intervention and at least one outcome variable were included. Each outcome was compared in both the large trial and meta-analysis. Two investigators worked independently and discrepancies were resolved by consensus with the help of a third investigator. Twelve large, randomized, controlled trials were identified to which 19 correspon-

ding meta-analyses were located. For a total of 40 primary and secondary outcomes, agreement between the two was only fair (Kappa: 0.35; 95% CI: 0.64). However, the difference in point estimates between the randomized trials and the meta-analysis was statistically significant for only 5 (12%) of the 40 comparisons. In each of these cases, one method found the effect of treatment to be statistically significant whereas the other method did not.

COMMENT

Randomized controlled trials (RCTs) with an adequate sample size are regarded as the 'best' way to answer questions on modes of treatment. However, it is not often practical or feasible to carry out trials with adequate sample size due to lack of patients, resources or other constraints. Though multicentric RCTs try to circumvent the problem of paucity of patients, they are very expensive. One method which is gaining importance is meta-analysis. This method of systematic review is more structured and statistically rigorous. Availability of computer-based literature search strategies have further simplified this process. This has also resulted in an 'abuse' of meta-analysis which has led to laying down of strict guidelines for meta-analysis.¹ One of the questions which has still not been answered completely is whether a properly done meta-analysis can provide the same information as a large RCT. This paper tries to address this issue.

One criticism of meta-analysis is that it not only incorporates the bias of individual studies but adds new sources of bias generated due to selection of studies (publication bias)² and the heterogeneity amongst them. By clearly specifying the journals used, their strategy and including all languages, the authors have