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.

REFERENCES

1 Johnson AG, Hosking SW. Appraisal of the management of bile duct stones. *Br J Surg* 1987;**74:**555–60.
2 Fiore NF, Ledniczyky G, Wiebke EA, Broadie TA, Pruitt AL, Goulet RJ, *et al.* An analysis of perioperative cholangiogrpahy in one thousand laparoscopic cholecystectomies. *Surgery* 1997;**122:**817–23.
3 Part F, Amouyal G, Amouyal P, Pelletier G, Grisch J, Choury AD, *et al.* Prospective controlled study of endoscopic ultrasonography and endoscopic retrograde pancreatography in patients with suspected common bile duct lithiasis. *Lancet* 1996;**347:**75–9.
4 Cotton PB. Endoscopic retrograde cholangiopancreatography and laparoscopic cholecystectomy. *Am J Surg* 1993;**165:**474–8.
5 Norton SA, Alderson D. Prospective comparison of endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in the detection of bile duct stones. *Br J Surg* 1997;**84:**1366–9.
6 Flowers JL, Zucker KA, Graham SM, Scovill WA, Imbembo AL, Bailey RW. Laparoscopic cholangiography: Results and indication. *Ann Surg* 1992;**215:** 209–16.
7 Rothlin MA, Schlumpf R, Largiader F. Laparoscopic sonography: An alternative to routine intraoperative cholangiography? *Arch Surg* 1994;**129:**694–700.
8 Rhodes M, Sussman L, Cohen MP. Randomised trial of laparoscopic exploration of common bile duct versus postoperative endoscopic retrograde cholangiography for common bile duct stones. *Lancet* 1998;**351:**159–61.
9 Julcher AS, Jurner MA, Lapps EW. Half fourier RARE MR cholangiopancreatography experience in 300 subjects. *Radiology* 1998;**207:**21–32.
10 Soto JA, Barish MA, Yucel EK, Siegenberg D, Ferrucci JJ, Chuttani R. Magnetic resonance cholangiography compared with ERCP. *Gastroenterology* 1996;**110:** 589–97.
11 Muxsella M, Barbalancely, Capparelli G, Magnetic resonance imaging in evaluation of the common bile duct. *Br J Surg* 1998;**88:**16–19.

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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 corresponding 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

tried to minimize the publication bias. The statistical methods used were appropriate and adequate for the study. Even though a formal sensitivity analysis was not performed, it was carried out wherever possible and necessary and indicated a robustness of the results.

The results of this study showed that if there were no RCTs, meta-analysis would have led to the adoption of ineffective treatment in 32% cases (alpha error) and rejection of effective treatment in 33% of instances (beta error). The study findings did not differ much from that of a previous study where the authors found a predictive value of 50%–67% for meta-analysis to predict results of large RCTs.[3]

Given this situation (the inconvenience in carrying out large RCTs and poor predictive value of the meta-analyses), what is the best way to obtain unbiased results? There is no simple and straight answer. The lesson of this article is that even results of meta-analysis should be interpreted with caution. One should go beyond the point estimates and confidence intervals. It is also important to look into each study and look for consistency. One should appraise each study separately. Misleading analyses can be avoided by following some basic principles such as considering meta-analysis as an observational study of evidence with similar steps taken for such a study, spelling out standardized outcome measures, adopting various methods of analysis (in fact, there is no single best method), proper presentation of the results/effects and doing a proper sensitivity analysis. Thus, it appears that interpreting meta-analyses would require more hard work by the readers and not less, as some people think.

REFERENCES

1 Spitzer WO. The challenge of meta-analysis. *J Clin Epidemiol* 1995;**48:**1–4.
2 Gregoire G, Derderian F, Le Lorier J. Selecting the language of the publications included in a meta-analysis: Is there a Tower of Babel bias? *J Clin Epidemiol* 1995; **48:**159–63.
3 Villar J, Carroli G, Belizan JM. Predictive ability of the meta-analyses of randomised controlled trials. *Lancet* 1995;**345:**772–6.

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