Liver biopsy under ultrasound control

Editor,—I read the recent occasional viewpoint by Shah et al (Gut 1999;45:628–629) with much interest. The authors describe their regional practice of mandatory real time ultrasound guidance for percutaneous liver biopsy in all cases of suspected diffuse liver disease. However, the published literature does not convincingly support the universal adoption of such a policy.

The only prospective randomised study cited in support of their protocol, by Lindor and colleagues,1 is open to a number of methodological criticisms. In particular, in an unspecified proportion of the patients randomised to ultrasound guidance, the procedure was not actually performed under direct guidance and was instead immediately preceded by a “biopsy room” ultrasound scan. The net result of this may have been to selectively raise the pre-biopsy scanning rates in the “ultrasound” cohort who were already more likely to have been previously scanned than the “blind” patients (76–78% v 67–68% in the respective groups).

In terms of the reduction in post-biopsy complications claimed by Lindor et al, the major impact was a reduction in hospitalisation due to pain. There was no statistically significant difference in the rates of bleeding or hypotension. The reduction in pain, in a non-blinded study, could have been due to several factors such as the patients’ perceptions of a “safer” guided scan or the potential for the physicians to more readily hospitalise patients with abdominal pain in the “blind” group.


Reply

Editor,—The technique used in the Lindor paper was somewhat of a hybrid between the “X marks the spot” (site usually marked in ultrasound departments, and the patient transferred to the ward for the procedure) and real time ultrasonography performed in the department under continuous visualisation. In their paper, Lindor and colleagues performed an ultrasound guided biopsy and performed the procedure within the department. Using Lindor’s method, the patient may move prior to biopsy, and intrahepatic vessels cannot be avoided. It is therefore an inferior technique compared with using the “real time ultrasound guided biopsy” method recommended by us. Nevertheless, the relevant statistical analyses from their study were as follows: two patients required hospitalisation in the ultrasound guided group with nine in the biopsy group (p=0.04), pain being the reason for admission in seven patients and pain plus hypotension in four. Bleeding occurred in nine patients in the ultrasound group versus 18 in the biopsy group (p=0.07). Simply stating that this last finding, which had a twofold difference between the groups was not significant and by implication not important, ignores what is a very relevant trend which did not reach the “magical” p<0.05 level due to insufficient numbers (that is, a type II error). As stated in our paper, a similar situation is probably relevant in the failure of studies to show significant differences in mortality due to the large numbers required. Clinical procedures are now the subject of appropriate monitoring. When clinicians fall below standard and imperil the safety of the patient, questions of competence are raised. The current concern about the safety of cardiac surgery has raised public awareness of the need for adequate training in all clinical procedures. The GMC and other professional bodies are looking at all aspects of day to day clinical practices and the moves towards structured training of junior doctors is part of these developments. Clearly there is a need to train gastroenterologists in endoscopic techniques—the need is no less for the practice of liver biopsy. “See one, do one, teach one” is an aphorism that will not stand up in the 21st century.

Dr Aspinall fails to mention what we consider to be one of the key results in the paper by Lindor et al; one of the patients in the blind biopsy group had to have emergency surgery for a damaged gall bladder. As stated in our paper, this situation can be virtually completely avoided by using real time ultrasonography. In the current climate, patients in whom a blind biopsy has led to perforation of the gall bladder, pleural cavity, or colon will seek legal redress for such blunders. When seeking consent, doctors must explain the details of the procedures and the safeguard margins associated with them. Failure to mention the added safety of using a guided rather than a blind biopsy could be seen as negligent. We hope that Dr Aspinall never faces this dilemma.

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Informed consent

Editor,—The phrase “informed consent” falls so readily from the pen that it is easy to forget that two distinct processes are involved: firstly, providing appropriate information and then obtaining consent from the patient. In attempting to combine these two steps, Shepherd and colleagues (Gut 2000;46:37–39) remove some of the patients’ essential safeguards. A multicentre retrospective study on 68,276 cases liver biopsy (approved training centre for European Accreditation in Gastroenterology) 1999;45:628–629.

The GMC advice3–5 points out in his gentle and thoughtful comment, “written information . . . is undoubtedly useful but it does not replace the over-riding need for doctors to speak with their patients . . .”. Neither the paper nor the commentary cite the GMC advice although they are quoted extensively in the British Society of Gastroenterology guideline on informed consent for endoscopy procedures. Particularly relevant is this: “obtaining informed consent cannot be an isolated event. It involves a continuing dialogue between you and your patients . . . . you should give . . . the patient time to ask questions”. However carefully prepared, a booklet cannot be appropriate for every patient and every circumstance. Pressing patients to “sign consent” in advance of meeting any endoscopy procedure is to deprive them of the opportunity to ask questions or seek reassurance. “If you are the doctor . . . undertaking an investigation it is your responsibility to discuss it with the patient . . .” although the job may be delegated to an appropriate person.

Giving information by post is desirable: requesting signed consent by that route is not.

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Editor,—Shepherd and colleagues (Gut 2000;46:37–39) offer a timely and thoughtful contribution to the increasingly loud debate in trusts about informed consent. As well as endoscopy, their example is relevant to other services offering invasive open access procedures, especially radiology. Their booklets address three problems: (i) that information regarding proposed procedures should be given in circumstances in which patients could not be perceived to be under duress to give consent; (ii) that the information is given, albeit indirectly, by one who is trained to perform the procedure; and (iii) that an explanation is given regarding risks as well as benefits, as is often not the case at present.

Neale’s commentary (Gut 2000;46:5–6) is, as one would expect, in many ways equally perceptive but he fails to take account of an essential aspect of open access services. As he makes clear, such a process of informing consent cannot address the problem of informing choice. Appropriate judgment about the information arrives through the post with an appointment for a particular procedure. However desirable it may be that such a choice should be an integral element of informed consent, the nature of an open access service dictates that the decision regarding the choice of the procedure must have been taken prior to the referral having been made. This raises two further issues: (1) how to arrive at an appropriate judgment to be used to decide the choice of the procedure; and (2) how to assess an acceptable level of risk for open access procedures in general and for the particular individual to whom a procedure is offered.

Neale’s example of ERCP, although not generally an open access procedure, serves to focus thinking about these unanswered questions but does not diminish the contribution of Shepherd and colleagues in enhancing the quality of information given to patients. The ratio of manpower to demand means that, for the foreseeable future, much as endoscopists may wish “to speak with their patients about options for further action” prior to offering procedures, attempting to do so in every case would impose unacceptable delays in their management.

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Reply

Editor,—Thank you for allowing me to see the correspondence regarding “informed consent”. Dr Bennett states that writing to inform a patient of what is involved in “open access” gastrointestinal endoscopy (including risks and benefits) is desirable but requesting patients to “sign consent” at home is not. He cites GMC advice that “informing consent cannot be an isolated event. It involves continuing dialogue between you and your patients… you should give… the patient time to ask questions.” In contrast, Dr Bruce states that “The expectation that manpower demand (for gastrointestinal endoscopy) means that much as endoscopists may wish to speak with their patients about… (this) would impose unacceptable delays in management.”

We were writing a commentary on informed consent I did not attempt to resolve these differences. As was stated in the BSG guidelines on informed consent, “In busy clinical practice it is not possible to satisfy NHS guidelines metacolonic mucosal permeability recognise the difficulties… Each unit must develop a code of practice suitable to its mode of operation… The law takes the view that the responsibility for obtaining informed consent lies with the endoscopist who is to perform the procedure…” But as the GMC concedes, “Where this is not practicable you may delegate (this responsibility)… to a person who is suitably trained and qualified; has sufficient knowledge…and understands the risks…”

The difficulty with open access endoscopy lies in the shared responsibility. The GP has assessed the patient and usually remains responsible for the patient’s care. I assume that consultant gastroenterologists who offer open access endoscopy instruct participating GPs carefully regarding indication, alternatives, risks, and potential benefits, thereby delegating responsibility. And as Shepherd and colleagues (Gut 2000;46:37–39) make clear, patients are not “pressed” to sign the consent form at home; they have the option not to sign until they have discussed the procedure with the endoscopist. Moreover, if the BSG guidelines are followed “…a qualified nurse should check the level of understanding and provide further explanation. The responsible endoscopist should deal with any last minute questions”.

Meanwhile, the value of open access endoscopy remains a subject for debate. It has been suggested that a one-stop dyspepsia clinic is a preferable means of practice. Such practice overcomes the problem of gastroenterologists “not speaking with patients about options”.

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Increased prevalence of methylenetetrahydrofolate reductase C677T variant in patients with IBD

Editor,—We read with interest the paper by Mahmud et al (Gut 1999;45:389–394). The study showed an increased prevalence of methylenetetrahydrofolate reductase (MTHFR) C677T variant in patients with inflammatory bowel disease (IBD). The C677T polymorphism is a known genetic cause of mild hyperhomocysteinaemia (hyper-Hcy) and may be associated with a variant degree of risk for thromboembolic disease in patients with IBD.

To confirm a higher prevalence of the C677T polymorphism, we investigated 9 patients with established IBD for this polymorphism compared with 1084 unselected newborns. DNA samples were genotyped for the MTHFR (C677T) mutation. Patients were categorised as homozgyous for the thermolability variant (TT), heterozygous for the wild-type variant (CT), or homozygous for the wild-type (CC).

In comparison between IBD patients and controls, the results were obtained using the chi-square test. Differences in onset of disease between patients with Crohn’s disease (CD)
and those with ulcerative colitis (UC) were compared using the Mann-Whitney test. A total of 16.2% (16/99) of IBD patients were homozygous for the C677T variant compared with 8.3% (90/1084) in the control group. This difference was statistically significant (p<0.009). When patients were stratified according to CD and UC, we found that homozygosity for the MTHFR C677T variant (TT) was present in 14.0% (7/50) of patients with CD and 18.4% (9/49) of those with UC. Both results were independently significantly higher than in the background population.

Onset of disease in carriers of the (TT) variant in CD and UC patients was 33.8 and 40.6, respectively, compared with 34.4 and 43.3 in non-carriers. This difference was not statistically significant. There was no correlation between disease activity indices of the IBD patients (Crohn’s disease activity index for CD and clinic activity index for UC) and carriers of the (TT) variants. Also, C reactive protein levels in IBD patients was independent of MTHFR gene prevalence.

Genome wide linkage screen of a large population of IBD patients found evidence of linkage of IBD to the short arm of chromosome 1 in all families investigated. It is interesting that the MTHFR gene is located on chromosome 1 (1p36.3). Additional loci on chromosomes 3, 7, and 16 are linked to IBD. The genetic basis of IBD is non-mendelian in nature and very complex. Unrecognised factors may therefore be important in the genesis of IBD. Further investigation of other factors is being carried out in our laboratory at present.

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Reply

Editor,—Thank you for the opportunity to comment on the letter of Dr Nielsen and colleagues. We are pleased that their data have confirmed our findings, as previously recorded (Gut 1999;48:389-94). We agree with their comment that the genetic basis of inflammatory bowel disease (IBD) is very complex. One point needs to be emphasised, namely that serum homocysteine levels were increased in our patients compared with controls, even when those patients who were homozygous for C677T polymorphism were excluded. This elevated level was present even when the effect of folate deficiency was excluded. This suggests that other polymorphisms as yet undiscovered may be present in one or other of the three enzymes responsible for removal of homocysteine in internal metabolism, namely methylenetetrahydrofolate reductase, methionine synthase, and cystathionine synthase. Accordingly, it is important to emphasise that all patients with IBD should receive regular therapy with 400 µg of folic acid daily.

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BOOK REVIEWS


Pediatric gastroenterology, and our knowledge about diseases of the small intestine in children, has grown rapidly over the last few years, owing to advances in the basic sciences, such as molecular genetics and, particularly, gut immunology. The purpose of this book is to provide the consultant paediatrician, as well as the trainee, with a review of the diseases of the small intestine in children. There are two major sections in the book: the first, more general, is focused on structure and mechanisms; the second, more specific, in which attention is paid to the commoner and more important specific disease entities. This fourth edition of a book published in the past by John Walker Smith, and now coauthored by Simon Murch, reflects the long clinical experience of the first author. At the same time, it offers a thorough review of the most recent literature. The long clinical experience of the senior author, which is particularly evident in the chapter dedicated to familial gastrointestinalis, is now integrated by the strong clinical and research interest of Dr Murch in mucosal immunology. The value of the chapters dedicated to matrix (a topic to which Dr Murch has significantly contributed with his own research), and to the immune system of the small intestine in the first section of the book, and to coeliac disease and Crohn’s disease in the second one, is a proof of this special competence. Also very good is the chapter on laboratory assessment, although less convincing is the part of the same chapter that discusses the chief symptoms of the child with gastrointestinal problems (diarrhoea, vomiting). The appendix on special milks is especially useful. Overall, the editorial quality of the book is high.

In conclusion, this book is a very valuable reference not only for paediatric gastroenterologists, but also for general practitioners, medical students, and dieticians.

R TRONCONE


I enjoyed looking at this book. The editors’ intention is that “as a moment comes when a surgeon may open it and consult an authority on a particular topic related to IBD surgery”. They have assembled an international group of contributors and there are excellent sections on history, surgical pathology, pouches, and Crohn’s surgery. There are some surprising omissions, however. A chapter on revision surgery for pouches that have gone wrong would have been timely, and a more thorough review of balloon dilatation and stents would have provided a look to the future. I think the sections on septic complications of pouches and Crohn’s disease should have been kept separate.

I was irritated by the lack of uniformity in the illustrations and drawings of procedures, and in places the text is very dense, for example, in the section on ileostomy.

A final point: there is only one chapter on medical management just when there is an explosion of new medical therapy. Joint physician/surgeon management is seen by many as the ideal, and surgical treatment cannot be viewed in isolation. This is a comprehensive and well illustrated book that will be a welcome addition to the shelves of specialists in IBD surgery.

N MORTENSEN


This is a substantial book edited by Dr Michael Wolfe with six of his colleagues acting as section editors. Many of the hundred or so contributors are members of the Boston home team. The others are from the key centres in North America with a smattering of contributors from Canada, Europe, Israel, and South America. This is in effect a GI textbook, but stripped largely of pathogenesis, pathophysiology, diagnosis, and differential diagnosis. Five main sections consider treatment of oesophageal, gastroduodenal, pancreatic or biliary, hepatic, and intestinal diseases.

The two column black and white presentation is relieved by good summary tables, with small clear diagrams and figures within the two column format. No flashy colour or bullet points here, but good solid information.

Clear instructions to the contributors and careful editing has produced consistent and well balanced chapters. In fact, the excellent contribution from Stephen Hannen deals briefly with an approach to history taking, physical examination, diagnostic studies, and laboratory investigation in patients with inflammatory bowel disease. This is followed by an overview of individual patient

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management and then the “meat” of the chapter reviews therapeutic options for ulcerative colitis and Crohn’s disease. The approaches to treatment in North America and in Europe were remarkably similar. International journals and meetings have narrowed the Atlantic Ocean to a trickle.

The chapter on non-variceal GI bleeding by Lichtenstein also provides remarkably consistent intercontinental advice, which is practical and appropriate and wherever possible evidence based. The detail is remarkable—for example, he has researched the history of iced saline lavage and concludes that water at room temperature is preferable.

I particularly liked the section on therapeutic endoscopy, which is a model of clarity and brevity. Whichever chapter is selected, the information is consistent, reliable, and well researched. The chapter by Nicholas La Russo on primary sclerosing cholangitis opens with an excellent and brief review of the genetics, pathogenesis, clinical features, diagnosis, and natural history, and then considers potential therapy of cupreusis, immunosuppressant agents, antifibrogenesis, cholestatic agents, surgery, and transplantation.

Even in complex areas such as the contribution by John Del Valle, concerned with the treatment of neuroendocrine tumours, for each specific syndrome there is a crisp, clear summary of recommended treatment. In summary, this is a remarkable, formidable achievement with consistent structure and advice, which is reliable and well based. Inevitably for a book of this size, the turnaround time results in the latest reference, which is predictable in light of the distinguished authorship, and of style. The last of these can have been achieved only by diligent editorial skills, and, I suspect, extensive rewriting. Although the authors are predominantly European, the spelling and approved drug names are from the opposite side of the Atlantic—a concession one assumes to the major potential market.

Mercifully, guidelines and patient care pathways are not favoured, whilst algorithms are sparingly dispersed. By contrast, the text is regularly punctuated with summarising tables and figures. These will be of particular interest to junior staff preparing their PowerPoint presentations. Hard pressed consultants will be no less enthusiastic, as the book provides a resource for rapid but comprehensive “revision” prior to a training session with the junior staff.

The chapters covering large bowel polyps and colorectal cancer will be of special value and interest to non-surgeons who have failed to keep abreast of the last decade’s developments in the classification and management of these tumours. Recommendations for endoscopic surveillance are discussed, although the authors admit that not all of these are fully supported by adequate evidence yet. Similarly, non-specialists requiring a review of liver transplantation and its place in the final year of the millennium, will be grateful to Ringe and his colleagues for their adroit contribution. The account of ulcerative colitis is a medicosurgical collaboration, which is a feature of many chapters. Medical therapeutic options are fully discussed, but one gains the impression that there may be a lower threshold for elective surgery in Germany than in the United Kingdom. This, however, is a rare example of the possible divergence between British and continental practice. Neville and Axon offer a balanced account of non-ulcer dyspepsia, but, regrettably, the editors have not taken the opportunity of giving this confusing terminology the red card. My men of the match are the Oxford trio for their chapter covering Crohn’s disease. I doubt there is a better succinct account currently in print.

A minor criticism is the rarity of speculations about future developments. It surely would have been timely to have made a few forays into the new millennium.

Although this book may not be in the champions’ league class, it is a thoroughly prestigious performance by a team that constantly has its eye on the ball.

M J LANCASTER SMITH


The last dinosaur disappeared from Earth over 66 million years ago, wiped out in some cataclysm that changed the world and its climate for ever.

Mankind gradually evolved, competing in a hostile environment, winning because of brain and hands. Knowledge and writing gave power; mankind strode on, erect, dignified. The pinnacle of hand-eye coordination, thoughtful and wise, stepped forth the surgeon.

Evolution continued, specialising, improving, learning, until from the chrysalis emerged the ultimate epiphany, a colorectal surgeon. Hungry, needing to learn, to understand the background, the proud evolution, the way of the tribe.

How to learn? Vast, illuminated, biblical scroll, or virtual, instant, ephemeral quantum world? Wonderful, musky smell, comforting weight, swirling flick of page, light low, old knowledge enters old eyes, stimulates old satisfaction, reveals new comprehension. But taut skin, restless energy, young ambition seeks flickering screen, a virtual world. A conundrum.

I am old, and thinning; a user of computers, but no bedfellow. At the frontier, I use journals and the library for reading, smaller books, concise, portable, incisive. However, for reference, to support an opinion, pursue a prejudice, grind an axe, to gainsay, then a large, lovingly written, luxuriously arranged book—a book and a half (indeed, two books); beautiful, admired, essential—just such books as these.

But I feel a gulf. I sit on the written side of that gulf, but close by I see a new generation, turning away, evolving further. Will they want such a book? There is no CD-ROM. Will they use other ways?

Although science changes rapidly, society and culture take much longer to adjust. Reading and book owning are as much cultural as they are efficient means of imparting knowledge, pleasantly, importantly, to be admired also on the shelf. I am confident they will read, they will own books, big books, books such as these books—fascinating, informative, a congratulation, and not the last dinosaur.

ROBIN PHILLIPS