Evidence-Based General Surgery

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Evidence-based surgery: do we need it, and can we get it?

Since the inception of the evidence based medicine movement, there have been regular attacks on surgeons for the perceived deficiencies of the evidence base in their speciality, and their apparent complacency in the face of this[1]. Surgeons have not always been their own best advocates in responding to this criticism, but some have attempted to mount a defence. This has comprised first an investigation of the true state of the surgical evidence base, and second a review and discussion of the particular features of surgery as a discipline which pose problems for randomised controlled trials. An analysis of general surgical work in a large UK hospital showed that only 24% of the treatments used were based on RCT evidence, compared with over 50% for inpatient general medicine[2]. A recent analysis of the illnesses and treatments most commonly encountered in general surgery suggested that less than 40% of operative treatments were amenable to study using an RCT design[3]. Some of the reasons suggested for this, such as the rarity or emergency nature of the conditions involved, are not wholly convincing, but others are important. It is useful to separate the historical features of this debate from those which continue to affect the prospects for a satisfactory evidence base for surgery in the future.

Historically, it has to be accepted that the majority of common general surgical operations were introduced before 1920, long before the importance of the randomised controlled trial was appreciated anywhere in the medical profession. On the other hand, most of the modern therapeutic armamentarium of the physician, dates from the era since World War 2, when pharmacology underwent a parallel and symbiotic growth with RCT

methodology. It is always hard to do randomised trials of well established treatments, because the attachment of both doctors and patients to the familiar prevents the level of open-minded doubt necessary to achieve "equipoise", that condition of uncertainty which allows a doctor ethically to randomise her patient between competing treatments. For this reason many operations (together with time-honoured medical treatments like morphine have largely escaped the rigours of the RCT versus placebo for their original indications.

So much for the history. The nature of treatment by surgical operation does however provide at least two good reasons for not performing RCTs (as well as a number of bad ones). Many of the conditions treated by surgery are of a mechanical nature, and in some cases (such as relief of mechanical bowel obstruction) the superiority of the mechanical solution offered by operation over non-treatment is self-evident. In many surgical scenarios, the benefits are so clear that no-one would consider a trial ethical or remotely sensible. Thus there was, and is, no question of a placebo-controlled trial of repair of inguinal hernia (in patients fit enough to be considered for one), relief of mechanical bowel obstruction or drainage of abscesses.

Surgery is a skilled, multistep process, and this makes RCT designs difficult to deliver in surgical studies, for two reasons. First, there is a learning process in every new operation, even for a fully trained surgeon unfamiliar with the particular procedure. Serious bias can easily be introduced if this is not acknowledged and measured or eliminated, especially for trials of new versus older procedures. Second, there is inherent variation in the way in which the procedure is performed by each different individual, and this cannot be eliminated. Surgeons stress the need for quality control in the technical aspects of any procedure under trial, but are acutely aware of the difficulty of the task. As in other areas in which the practitioner can be regarded as part of the treatment, it may be appropriate to stratify surgical trials by surgeon: this alone is not enough, however. Good surgical quality control means having valid objective measures which can demonstrate that an operation has been carried out according to predefined principles. This is a great deal more demanding than measuring patient compliance with drug treatment, but even more important: until recently, it was largely absent. Much of the cynicism expressed by surgeons about RCTs stems from their concern about this inability of crude designs to acknowledge the critical importance of quality in defining surgical outcome. We know that large variations in outcome are observed between surgeons performing similar operations in the same population[4]. If these do indeed reflect differences in the quality of surgery, it is salutary to note that they may be significantly greater than the expected differences between groups from ancillary treatments such as chemotherapy.

So surgery can be said to have a less secure evidence base than internal medicine, albeit for understandable reasons. If we look forward rather than back, this poses two questions. First, how do we evaluate and use an evidence base which is currently poor in RCTs, but rich in treatments for which a placebo-controlled trial would be unthinkable? Second, how can we create a more secure base for the future, taking into account the real problems outlined above? Whether we need to tackle these questions is no longer a question worth asking. The public demand for evidence-based justification of medical practice in all specialities is becoming more and more starkly expressed in the actions and statements of the courts and of political leaders. It is no longer possible to appeal to the mystique of professional expertise, when asked to justify our decisions - or our results. The less secure the evidence base for our practice, the less likely it is to be able to withstand pressure from public and political voices. The changes demanded by those with a better understanding of public opinion than of medical practice are unlikely to be beneficial in the long run. Surgeons, like other doctors, need evidence-based medicine now, because the alternative is policy-based medicine.

So we need evidence-based surgery. Can we get it? Yes, but it will be significantly more difficult than in some other branches of medicine. To address the first of the questions raised above, we need to take a serious and systematic look at the best way to evaluate what we have in terms of surgical evidence. We wish we had more RCTs, but we don't. It will take years to reverse this situation, and until then we must either make the best efforts we can to analyse the available evidence from largely non-randomised studies or adopt an attitude of staunch agnosticism. I believe the former is the more sensible approach, but it represents a significant development in the scope of evidence based medicine. To achieve it we need rules, themselves well researched and validated, for determining the quality of the non-randomised studies in which surgery abounds. We need to develop a system of description which allows us to make an estimate of the efficacy of a treatment based on the best of this data, together with an estimate of the relative quality of this evidence. This is the best we can hope to achieve from the starting point we have been given, and it is better than nothing. We surgeons will need help in delivering it, particularly from clinical epidemiologists and statisticians. In order to provide this, many of them will need to put aside misgivings about supporting what they will probably see as a validation of second-class evidence. Using what we have should not be seen as such, and the best guarantee to those with concerns should be the efforts of surgeons to improve the quality of clinical surgical research in the future.

There is an important task to be undertaken in defining the current state of the evidence in surgery, and in particular the areas in which there is both an important unanswered question and a realistic means to performing the

studies to answer it. As we define the most important areas of ignorance, we need to develop the tools to investigate them. There are ways to address the practical difficulties peculiar to surgery, and they need to be taken seriously and instituted. It may require log-books for consultant surgeons, plus site visits from co-ordinating experts, but it is, in principle, possible to overcome the problems of the learning curve. Satisfactory quality control may need similar unfamiliar measures, such as detailed guidance to define what variations in technique are acceptable within the trial, and submission of case notes, videos or x-rays to confirm correct technique. All of this will make surgical trials much more difficult and expensive to run. If this is to succeed it will need political support for the funding of a clinical research infrastructure with the resources to do the job properly. This is perhaps the most difficult obstacle of all, but it must be faced. It would make no sense to take the alternative approach of failing to resource the development of better surgical trials, and then criticising surgeons for not performing them. Give us the tools and we will finish the job.

Peter McCulloch
Liverpool, April 1999-04-13

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[1] Horton R. Surgical Research or Comic Opera? Questions, but few answers. Lancet 1996; 347: 984-5.

[2] Howes N, Chagla L, Thorpe M & McCulloch P. Surgical Practice is Evidence-Based. Brit. J. Surg. 1997; 84: 1220-1223

[3] McLeod RS, Wright JG, Solomon MJ, Hu X, Walters BC & Lossing Al. Randomized controlled trials in surgery: Issues and problems. Surgery 1996; 119: 483-6.

[4] McArdle CS & Hole D. Impact of variability among surgeons on postoperative morbidity and mortality and ultimate survival. Brit. Med. J. 1991; 302: 1501-5.

A. Diagnosis

Clinical scenario

You see a 44 year old lady in your multidisciplinary follow-up breast clinic. She had a wide local excision and axillary clearance for a 1.7cm Grade 2 ductal carcinoma 2 years ago. Two of 17 axillary nodes were positive for tumour, and she recieved postoperative radiotherapy to the breast tissue, sandwiched with 6 cycles of CMF chemotherapy. Ever since the radiotherapy, the area under the surgical scar has been very firm. A routine follow-up mammogram show increasing density and architectural distortion in this area, and there is a concern about local recurrence. A core biopsy was unsatisfactory because of the very hard consistency of the tissue. Because of the size and site of the mammographic abnormality, a diagnostic excision biopsy is likely to leave a very poor cosmetic result. The patient is very keen to avoid a mastectomy if at all possible. You explain that you cannot be sure whether she has local recurrence or not. She asks (a) What is the best method of investigating this without further surgery? (b) How good is this method?

Together, you formulate the question:
In a patient with a history of breast cancer and breast conserving surgery what is the best method for detecting local recurrence? AND How accurate is it?

You search Medline using the terms 'breast neoplasms' and 'screening' and 'mastectomy'. You find an article by Drew et al and decide to review it. Ann Surg Oncol1998;5:265-70 (www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9607630&dopt=Abstract)

Read the article and decide,

1. Are the results of this study of prognosis valid?
2. Are the results of the study important?
3. Can you apply this valid, important evidence about prognosis to the treatment of your patient?

Completed Worksheet

Citation

Drew PJ, Kerin MJ, Turnbull LW, Imrie M, Carleton PJ, Fox JN & Monson JRT. Routine screening for local recurrence following breast-conserving therapy for cancer with dynamic contrast-enhanced magnetic resonance imaging of the breast. Ann Surg Oncol 1998;5:265-70. (www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9607630&dopt=Abstract)

Are the results of this diagnostic study valid?

Was there an independent, blind comparison with a reference ("gold") standard of diagnosis?	**Yes. The standard used (mammography plus palpation, but without routine use of ultrasound) could be criticised as suboptimal, but is representative of contemporary specialist practice in the UK.**
Was the diagnostic test evaluated in an appropriate spectrum of patients (like those in whom it would be used in practice)?	**Probably. The new test (MRI) was offered to women undergoing breast-conserving therapy. The paper does not mention any exclusions, and it does not say how many women refused to take part, nor whether they were different from those who participated.**
Was the reference standard applied regardless of the result	**Yes**

of the new diagnostic test?	

Are the valid results of this diagnostic study important?

	Outcome		
MRI Result	CANCER	BENIGN	LIKELIHOOD RATIO
Positive	9 / 9	6 / 96	16*
Negative	0 / 9	90 / 96	0

Can I apply this valid, important evidence about a diagnostic test in caring for my patient?

Is the diagnostic test available, affordable, accurate and precise in my setting?	**Is the diagnostic test available, affordable, accurate and precise in my setting?**
Can I generate a clinically sensible estimate of my patient's pre-test probability of having local recurrence?	**The scenario suggests that there is enough clinical thickening to raise concern, but no convincing features of recurrence. From experience, I would guess at a pretest probability of cancer of maybe 20% in this situation.**
Will the resulting post-test probabilities affect my management and help the patient?	**The pre-test odds are 1:5, x the LR of 16 = post test odds of 16:5 or 3.2:1. This is equivalent to a post-test probability of having recurrent cancer of 76% if the MRI is positive: this would certainly be enough to recommend biopsy.**
Would the consequences of the test help my patient?	**Yes, provided she was not so determined to avoid surgery that nothing could sway her.**

Clinical Bottom Line

This looks like a considerable advance for the diagnosis of local recurrence after breast conserving surgery. We need to be sure that it can be done everywhere, not just by one group of experts.

Breast cancer recurrence: MRI may help in the diagnosis

Clinical Bottom Line

MRI may be helpful in the diagnosis of local recurrence of breast cancer.

Citation

Drew PJ et al. Routine screening for local recurrence following breast-conserving therapy for cancer with dynamic contrast-enhanced magnetic resonance imaging of the breast. Ann Surg Onc 1998;5:265-70. (www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9607630&dopt=Abstract)

Clinical Question

In a patient with a history of breast cancer and breast conserving surgery, what is the best method for detecting local recurrence?

Search terms

breast cancer and recurrence and screening in Medline

The study

The Study Patients: women with breast cancer undergoing breast conserving surgery

Study Feature	Yes	No	Can't tell
Independent?	X		
Blind?	X		
Standard applied regardless of test result?	X		
Appropriate spectrum..?			X

Target disorder and Gold Standard: mammography and palpation
Diagnostic test: MRI

The evidence

	Disorder				
	Present		**Absent**		
Test Result	Num.	Prop.	Num.	Prop.	LR
Positive	9	a	6	b	16.00
Negative	0	c	90	d	0.00

Sensitivity: 100%; CI: 100 to 100
Specificity: 94%; CI: 89 to 98
Prevalence: 9%; CI: 3 to 14
Positive Predictive Value: 60%; CI: 51 to 69
Negative Predictive Value: 100%; CI: 100 to 100

Comments

Small numbers
Kill or Update by: 2001

Particular to my patient:
Pre-test probability: 20%
Test Result Post-test probability
Positive 80%
Negative 0%

B. Prognosis

Clinical scenario

A seventy-five year old retired headmistress sees you in the clinic after a recent emergency admission with a peridiverticular abscess. This was successfully managed with five days of intravenous antibiotics, but your patient is knowledgeable and understands that the underlying bowel condition is unchanged. She asks what the risks of a second emergency admission are for someone in her position. She is clearly weighing up the possibility of undergoing elective surgery to prevent any recurrence. You tell her you will review the literature to find out the chances of repeated severe complications in patients who have had one emergency admission for a complication. You explain that the risks are of recurrent peridiverticulitis, abscess or phlegmon formation, perforation, obstruction or haemorrhage. You formulate the query: In patients admitted as an emergency with complications of diverticular disease, what is the risk of a second emergency admission for further complications?

You search Medline using the terms 'diverticulosis' and 'complications' and find a relevant article. Br J Surg 1994;81:733-5. (www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8044566&dopt=Abstract)

Read the article and decide,

1. Are the results of this study of prognosis valid?
2. Are the results of the study important?
3. Can you apply this valid, important evidence about prognosis to the treatment of your patient?

Completed Worksheet

Citation

Farmakis N, Tudor RG & Keighley MRB. The 5-year history of complicated diverticular disease. Brit. J. Surg. 1994; 81: 733-5.

Are the results of this prognosis study valid?

Was a defined representative sample of patients assembled at a common (usually early) point in the course of their disease?	**Yes. All patients were studied from the time of first emergency admission for complications of diverticular disease.**
Was patient follow-up sufficiently long and complete?	**Only 120 of 176 (68%) cases were successfully traced, and follow-up was a minimum of 5 years, by which time 1/3 of the patients had died. The median follow-up was not recorded.**
Were objective outcome criteria applied in a "blind" fashion?	**Questionnaires were sent to the GPs of all patients with an index emergency admission, asking about recurrent admissions, symptoms, operations, deaths and cause of death.**
If subgroups with different prognoses were identified, was there adjustment for important prognostic factors?	**Subgroups were not identified.**
Was there validation in an independent group (test set) of patients?	**No.**

Are the valid results of this prognosis study important?

How likely are the outcomes over time?	**Death from diverticular disease: 1.7% per year. Further serious complications: 6.5% per year. Readmission with further complications: 2.5% per year*. Continuing symptoms at 5 years: 33%.**
How precise are the prognostic estimates?	**95% Confidence intervals are: for death, 0 - 3.9% per year. For further serious complications, 2.1 - 10.9%**

	per year. For readmission 0 - 5.3% per year. For continuing symptoms at 5 years: 24.6 - 41.4%
Can you apply this valid, important evidence to the management of your patient?	
Were the study patients similar to your own?	**As far as we can see, yes.**
Will this evidence make a clinically important impact on what you offer to or tell your patient?	**Yes**

Additional Notes

1. The 77 patients in this cohort who had emergency colectomy had a very low risk of further complications (2/77), whereas 37 of the 43 who had conservative treatment had further severe complications.
2. No data is given about the mortality of emergency colectomy in this group. In the contemporary study of Sarin and Boulos (Ann. Roy. Coll. Surg. Eng. 1994; 76: 117-20.) this was 12%. This paper quotes a similar rate of re-admission (2% per year), and agrees that those who had a colectomy are at very low risk for recurrent problems.
3. The incomplete follow-up and multi-centre nature of the study suggest possible sources of selection bias.

Clinical Bottom Line

There is a significant risk of further severe complications in patients similar to mine. There is therefore a case for elective prophylactic resection, and some indirect evidence that it is likely to be effective: it is also likely to carry a significant mortality rate. An RCT is needed to determine the balance of risks and benefits in a defined patient group.

Diverticulitis - Risk of recurrent admission and death after first emergency admission

Clinical Bottom Line

Diverticulitis - Risk of recurrent admission and death after first emergency admission.

Citation

Farmakis N et al. The 5-year history of complicated diverticular disease. Br

J Surg 1994;81:733-5. (www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8044566&dopt=Abstract)

Clinical Question

In patients admitted as an emergency with complications of diverticular disease, what is the risk of a second emergency admission for further complications?

Search terms

diverticular disease, emergency admission in Medline

The study

The Study Patients: patients admitted for first time with emergent complications of diverticulitis

Prognostic Factor: emergency admission

The Outcome: death and readmission

Study Feature	Yes	No	Can't tell
Well-defined sample at uniform (early) stage of illness?	X		
Follow-up long enough?	X		
Follow-up complete?		X	
Blind and objective outcome criteria?	X		
Adjustment for other prognostic factors?		X	
Validation in an independent "test-set" of patients?		X	

The evidence

Prognostic Factor	Outcome	Time	Measure	Confidence Interval
emergency admission	readmission	1 year	2.5%	0 to 5.3%
Emergency admission	death from diverticular disease	1 year	1.7%	0 to 3.9%

Comments

inadequate follow-up (less than 80%)
Kill or Update by: 2001

C. Therapy

Clinical scenario

An obese 47 year old barrister is admitted under your care as an emergency with acute abdominal pain, and a diagnosis of acute gallstone-associated cholecystitis is made on ultrasound examination. You explain the likelihood of recurrent attacks and recommend surgery. Your patient is determined to return to work as soon as possible. Because of this, she indicates her preference for an immediate rather than a delayed cholecystectomy. You point out that the recovery time is likely to be longer if she has a conventional (non-mini) open cholecystectomy than if she has a laparoscopic procedure. She asks you whether the option of immediate laparoscopic operation is possible, as this seems to be the option which would allow her to return to work in the shortest time. You tell her that acute cholecystitis has, until recently, been regarded as a contraindication to laparoscopic cholecystectomy (LC), but that it is now being tried. She asks what the evidence is about its safety and efficacy. You decide, after talking with her further, that what she is seeking is evidence about the percentage of cases in which early laparoscopic cholecystectomy is feasible, and about whether it is as safe as early open cholecystectomy (has an equivalent incidence of serious and non-serious complications). You formulate the question: In people with acute cholecystitis can LC be carried out, and is the complication rate greater or less than that for open cholecystectomy?

A Medline search (using the terms 'laparascopic cholecystectomy' and 'open cholecystectomy') yields a recent Lancet paper, reporting a randomised controlled trial of Laparoscopic versus open (conventional incision) cholecystectomy in acute cholecystitis Lancet 1998; 351: 321-5. (www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9652612&dopt=Abstract)

Read the article and decide,

1. Is the evidence from this randomised trial valid?
2. If valid, is it important?
3. If valid and important, can you apply the evidence in caring for your patient?

Completed Worksheet

Citation

Kiviluoto T, Siren J, Luukkonen P & Kivilaakso E. Randomised trial of laparoscopic versus open cholecystectomy for acute and gangrenous cholecystitis. Lancet 1998; 351: 321-5. (www.ncbi.nlm.nih.gov/entrez/query.fcgi?

cmd=Retrieve&db=PubMed&list_uids=9652612&dopt=Abstract)

Are the results of this therapy study valid?

Was the assignment of patients to treatments randomised?	**Yes**
Were all patients who entered the trial accounted for at the conclusion? Were they analysed in the groups to which they were randomised?	**Yes**
Were patients and clinicians kept blind as to which treatment was being received?	**No**
Aside from the experimental treatment, were the groups treated equally?	**The management of suspected common bile duct stones was different in the two groups: This may have prolonged the mean operating time of the patients undergoing open cholecystectomy, because 60% of them had an operative cholangiogram added to the procedure.**
Were the groups similar at the start of the trial?	**Yes**

Are the valid results of this randomised study important?

End points considered: hospital morbidity, length of hospital stay, length of time off work, percentage of LC converted to OC.

It is worth pointing out that, whilst physicians are usually interested in the percentage benefit from their treatments, and the percentage of their patients in which this occurs, there are many situations in which surgeons can reasonably expect a 100% response rate in all of their patients (as here, where it is impossible to get cholecystitis after the operation). In these situations, comparisons of different techniques must necessarily concentrate on minimising the adverse effects of the surgery. Many surgical publications deal mainly with these effects: The commonly used, generally applicable measures of adverse effects are:

- Mortality

- Morbidity (defined as any adverse event related to the treatment, but usually applied only to COMPLICATIONS, defined as adverse effects of treatment which are NOT INEVITABLE)
- Hospital Stay
- Pain (from the operation)
- Time off Work

Morbidity and Mortality can be expressed as rates, and an NNT calculated. Durations can usefully be expressed as an index which is 1/duration. Hospital stay can then be compared using the ratio of indices e.g. Hospital Stay Index for LC (median) = 1/4 = 0.25. HSI for OC is 1/6 = 0.167. The Hospital Stay Ratio between the two is therefore 6/4 = 1.5. Another method (useful only if everyone can agree on a suitable figure) is to calculate the percentage of cases in which the duration involved exceeded a given figure, and the NNT to prevent one instance of this calculated. This is the procedure used here for duration of time off work.

Calculations

1. Hospital Morbidity

OC Complication Rate (CER)	LC Complication Rate (EER)	RRR	ARR	NNT
42%	3% (19%)*	93% (55%)*	38% (23%)*	2.6 (4.3)*

95% CI on NNT = +/- 0.25 (0.21)
* (IF CONVERSION TO OC IS COUNTED AS A COMPLICATION)

2. Length of hospital stay

OC median stay (CER)	LC median stay (EER)	HSR
6 days	4 days	1.5

3. Length of time off work

OC sick leave > 2/52* (CER)	LC sick leave > 2/52* (EER)	RRR	ARR	NNT
100%	40%	60%	60%	1.67

95% CI on NNT = +/- 0.06
* arbitrary cut-off point chosen by reviewer

4. Percentage of LC converted to OC

Calculations inapplicable: rate was 16%

Can you apply this valid, important evidence in caring for your patient?

Do these results apply to my patient?	
Is your patient so different from those in the trial that its results can't help you?	**No: similar**
How great would the potential benefit of therapy actually be for my patient?	
Method I: Risk of (complications or conversion to OC) in my patient relative to risk in the trial, expressed as a decimal : presumed to be 1.	NNT/f = 4.3
Method II: Your patient's expected event rate if they received the control treatment:	1 / (PEERxRRR) = 1 / (42%x55%) = 4.32
Are my patient's values and preference satisfied by the regimen and it's consequences?	Needs to be assessed in each patient, but YES for the patient described.

Clinical bottom line

This was a small study, and the difference in the rate of complications between the groups was really quite surprising, since most uncontrolled reports have shown the biggest risk of complications is amongst LC patients who undergo conversion to OC. The LC were all carried out by experts, whilst the OC were mostly carried out by trainees. As with many surgical trials, adequate blinding could not be carried out. This may have influenced length of hospital stay (see Squirrel et al, Surgery 1998; 123: 485-95 [www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9591000&dopt=Abstract]). Overall, the conclusion that LC is better has to be regarded with some caution.

Acute Cholecystitis - Lap chole may be as safe as open chole

Clinical Bottom Line

Acute Cholecystitis - Lap chole may be as safe as open chole

Citation

Kiviluoto T et al. Randomised trial of laparoscopic versus open cholecystectomy for acute and gangrenous cholecystitis. Lancet 1998;351:321-5. (www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9652612&dopt=Abstract)

Clinical Question

In patients with acute cholecystectomy, what is the complication rate of laparascopic cholecystectomy versus open cholecystectomy?

Search terms

laparascopic cholecystectomy and open cholecystectomy and cholecystitis in Medline

The study

Non-blinded randomised controlled trial without intention-to-treat.
The Study Patients: patients with acute cholecystitis
Control group (N = 31; analysed): open cholecystectomy
Experimental group (N = 32; analysed): lap chole

The evidence

Outcome	CER	EER	RRR	ARR	NNT
Complication from surgery	42%	3%	93%	.39	(2 to 5)
Complication including conversion to open chole	42%	19%	55%	.23	4 (2 to 106)

Comments

1. small study
2. lap chole carried out by experts while open chole mostly carried out by trainees

Kill or Update By: 2001

D. Harm

Clinical scenario

You are referred a 68 year old retired company director with cancer of the proximal stomach. He has angina on moderate effort, is moderately obese (despite recent weight loss) and has a history of excessive alcohol consumption, ceasing about seven years previously. He asks you what type of surgery is

available for his condition. Staging investigations including CT and laparoscopy have not shown any liver or peritoneal metastasis, nor any invasion of adjacent organs. You therefore recommend a total gastrectomy with curative intent. He has heard about the controversy over the risks and benefits of extended lymphadenectomy in the Japanese style, and has asks whether you would recommend the Japanese operation for him. You explain that a survival benefit has not been proven for this surgery, although many surgeons remain enthusiastic. He asks, very reasonably, whether the increased risk attributed to the Japanese operation is also unproven. Together, you formulate the question: Is radical lymphadenectomy more dangerous than conventional resection in patients with gastric cancer?

A Medline search (using the terms 'gastric cancer' and 'lymph node excision' yields two recent randomised controlled trials looking at this question. You choose the first of these Lancet 1995; 345: 745-8. (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7891484&dopt=Abstract)

Read the article and decide,

1. Are the results of this harm study valid?
2. Are the results of the harm study important?
3. Should these valid, important results change the treatment of your patient?

Completed Worksheet

Citation

Bonenkamp JJ et al. Randomised comparison after D1 and D2 dissection for gastric cancer in 1996 Dutch patients. Lancet 1995;345:745-8. (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7891484&dopt=Abstract)

Are the results of this harm study valid?

Were there clearly defined groups of patients, similar in all other important ways other than exposure to the treatment (D2 resection).	**Yes. All subjects taking part in a randomised trial, for entry to which they had to be fit to receive either D1 or D2 operation, and potentially curable as judged preoperatively. They could, however, be excluded for inoperability at laparotomy, after randomisation. There is a slight risk that surgeons might exclude more patients on these grounds if they were assigned to an operation THEY believed to be more dangerous. There**

	were slightly more exclusions for inoperability in the D2 group (163) than in the D1 group (142).
Were treatment exposures and clinical outcomes measures in the same way in both groups? Was assessment objective, or blinded as to treatment exposure.	**Partly. Postoperative death was an objective measure. Complications and reoperations were recorded in the knowledge of the treatment given. This knowledge may have affected the decision to class an incident as a complication, or to perform a re-exploration.**
Was the follow-up of study patients complete and long enough?	**Yes.**
Do the results satisfy some "diagnostic tests for causation"?	
Is it clear that exposure preceded outcome?	**Yes: operation preceded death in all cases!**
Is there a dose-response gradient?	**No. Patients either got D1 or D2 surgery.**
Is there positive evidence from a "dechallenge-rechallenge" study?	**Not possible in surgery.**
Is the association consistent from study to study?	**Yes: similar results in Cuschieri et al, Lancet 1996; 347: 995-9**
Does the association make biological sense?	**Yes, in that bigger surgery is usually more dangerous surgery.**
BUT: The important question of the learning curve for a surgical operation was inadequately addressed by both this and the other large trial. D1 surgery was widely practised in the Netherlands before the study, but the "supervising surgeons" got only 1-3 opportunities to practise the D2 technique with expert supervision before supervising others doing it. There is evidence that minimising the complication rate for D2 resection may take 20-25 operations (Parikh et al, 1996). **AND: There was a very clear association between**	

additional resection of the spleen or distal pancreas and mortality on multivariate analysis. After allowing for this, the association of mortality with extended lymph node dissection disappeared.

Are the valid results of this harm study important?

Adverse Outcome (postoperative death)

		Present	Absent
Exposed to the treatment? (D2 resection)	Yes	13%	87%
	No	6.5%	92.5%

Relative Risk = 13/6.5 = 2.0 (p=0.04)

Should these valid, potentially important results of a critical appraisal about a harmful treatment change the treatment of your patient?

Can the study results be extrapolated to my patient?	**If you accept them at face value, yes. You may also interpret them as suggesting that extended nodal dissection by a suitably experienced surgeon, avoiding additional organ resection, may carry no increased risk.**
What are your patient's risks of postoperative death?	**If we assume our patient is like the average study patient (and we are like the average study surgeon!) then his Absolute risk is** **13%-6.5% = 6.5%: 1/6.5% = 15**
What are your patient's preferences, concerns and expectations from this treatment?	**Need to be determined.**
What alternative treatments are available?	**Since the evidence against conventional D2 looks strong enough to be worrying, you could offer him D2 with preservation of the spleen and pancreas (if technically possible) or D1 resection.**