

The term “evidence-based medicine” was first coined by Sackett and colleagues as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.”<sup>1</sup> The key to practicing evidence-based medicine is to apply the best current knowledge to decision-making for individual patients. Medical knowledge is continually and rapidly expanding and it is impossible for an individual clinician to read all the medical literature. For clinicians to practice evidence-based medicine, they must have the skills to read and interpret the medical literature so that they can determine the validity, reliability, credibility, and utility of individual articles. These skills are known as critical appraisal skills. Generally, critical appraisal requires that the clinician have some knowledge of biostatistics, clinical epidemiology, decision analysis, economics, and clinical knowledge.

Beginning October 2005 the American College of Surgeons will join with the Canadian Association of General Surgeons to sponsor a program entitled “Evidence Based Reviews in Surgery (EBRS),” supported by an educational grant from Ethicon Inc. and Ethicon Endo Surgery Inc. The primary objective of this initiative is to help practicing surgeons improve their critical appraisal skills. During the academic year, 8 clinical articles are chosen for review and discussion. They are selected not only for their clinical relevance to general surgeons but also because they cover a spectrum of issues important to surgeons; for example, causation or risk factors for disease, naturally history or prognosis of disease, how to quantify disease (measurement issues), diagnostic tests and the diagnosis of disease, and the effectiveness of treatment. Both methodologic and clinical reviews of the article are performed by experts in the

relevant areas and posted on the EBRS website. As well, a listserv discussion is held where participants can discuss the monthly article. Fellows and candidates of the College can access Evidence Based Reviews in Surgery through the American College of Surgeons website ([www.facs.org](http://www.facs.org)). All journal articles and reviews are available electronically through the website. Currently we have a library of 40 articles and reviews that can be accessed at any time. Beginning in October, a new set of articles will be available each month until May. Surgeons who participate in the current (modules) packages can receive CME credits by completing a series of MCQ. For further information about EBRS the reader is directed to the ACS website or should email the administrator, Marg McKenzie at [mmckenzie@mtsinai.on.ca](mailto:mmckenzie@mtsinai.on.ca).

In addition to making the reviews available through the ACS and CAGS websites, 4 the reviews are published in condensed versions in the *Canadian Journal of Surgery* and the other 4 will be published in the *Journal of the American College of Surgeons* each year. This month’s article by Lindsay and colleagues entitled “A Randomized Controlled Trial of Fibrin Glue versus Conventional Treatment for Anal Fistula” is the first in the series for JACS. There are 13 articles that have been published previously in the *Canadian Journal of Surgery*. We hope readers will find EBRS useful in improving their critical appraisal skills and also keeping abreast new developments in general surgery. Comments about EBRS may also be directed to [mmckenzie@mtsinai.on.ca](mailto:mmckenzie@mtsinai.on.ca).

## REFERENCES

Evidence Based Medicine Working Group. Evidence-based medicine. JAMA 1992;268:2420–2425.

## SELECTED ARTICLE

### A Randomized, Controlled Trial of Fibrin Glue vs. Conventional Treatment for Anal Fistula

Lindsey I, Smilgin-Humphreys MM, Cunningham C, et al; Dis Colon Rectum 2002;45(12):1608–1615.

### Reviewed by

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## ABSTRACT

**Question:** Is there a difference between fibrin glue and conventional treatment for low and high anal fistulas?

**Design:** Randomized controlled trial

**Setting:** Single center trial, Oxford UK

**Patients:** Forty-two patients with simple fistulas (n = 13) and complex fistulas (high Crohn’s and low fistulas with compromised sphincters) (n = 29) were assigned to

either fibrin glue or conventional treatment (fistulotomy or loose seton insertion with or without subsequent advancement flap). Patients with rectovaginal fistulas and anal fistulas associated with chronic cavities, acute sepsis, and side branches were excluded.

**Interventions:** In patients randomized to fibrin glue, the fistula tract was curetted, irrigated with hydrogen peroxide and then the fibrin glue filled the tract until a “blob” was seen at the internal opening. Those in the conventional treatment group were treated according to the center’s standard fistula treatment. This consisted of fistulotomy, insertion of a loose seton and possibly advancement flap at a later date.

**Main Outcomes:** Fistula healing as defined as “complete cessation of drainage and the absence of complications.”

**Results:** Fibrin glue healed 3(50%) of 6 and fistulotomy 7 (100%) of 7 simple fistulas (difference, 50%; CI, 10% to 90%;  $p = 0.06$ , Fischers exact probability test). Fibrin glue healed 9 (69%) of 13 and conventional treatment 2 (13%) of 16 complex fistulas (difference, 56%; 95% CI; 25.9% to 86.1%;  $p = 0.003$ , Fischers exact probability test.) There were no significant changes in baseline incontinence scores, maximum resting pressures or squeeze pressures between study arms. In the simple fistula group, return to work was quicker in the fibrin glue arm but pain scores were similar and satisfaction scores were higher in the conventional treatment arm. In the complex fistula group satisfaction scores were higher in fibrin glue arm.

**Conclusions:** There is no advantage to fibrin glue over conventional treatment for simple fistulas, but fibrin glue healed more complex fistula than conventional treatment with a higher patient satisfaction.

**Commentary:** This is a single institution randomized controlled trial designed to compare the outcomes of both simple and complex anal fistulas treated with fibrin glue or operation. Eligible patients were assessed intra-operatively to determine the complexity of the fistula and whether the fistula was amenable to treatment with fibrin glue before being randomized to either fibrin glue or conventional treatment (fistulotomy or seton insertion +/- subsequent advancement flap). A total of 42

patients were included in the trial; 29 patients had complex fistulas and 13 had simple fistulas. Nineteen were randomized to fibrin glue and 23 to the surgical arm. At 12 weeks, overall 12 19 (63%) patients treated with fibrin glue versus 9 23 (40%) patients treated with surgical therapy had healed fistulas. Interestingly, healing with fibrin glue was better in the complex fistula group (69%) compared to the simple fistula group (50%).

In this study, Lindsay and colleagues evaluated a novel yet simplistic approach to the treatment of both simple and complex fistulas. The majority of fistulas-in-ano can be safely dealt with by a simple laying open technique or so-called fistulotomy. But complex fistulas may transverse significant muscle and operation may result in significant postoperative incontinence. Furthermore, fibrin glue has been advocated even in simple fistulas because any procedure that avoids division of any sphincter muscle and results in permanent fistula healing deserves exploration.

Although the investigators deserve credit for tackling a difficult surgical problem and performing a randomized controlled trial, there are some limitations to this study. First the sample size is small. In calculating the sample size, the authors anticipated a proportional treatment effect of 0.45 (i.e.: 75% versus 30% healing). It is not stated which treatment the authors anticipated to have better efficacy. It would seem unlikely that they would have performed a trial if they anticipated a success rate of only 30% in the fibrin glue group (i.e.: 45% lower than standard treatment). On the other hand, if they anticipated the success rate would only be 30% in the surgical group, it is not in keeping with published success rates of fistulotomy. By any standards, a difference in the treatment effect size of 45% is large. The authors fail to justify these rates leaving the reader in a quandary why these numbers were chosen and suspecting that the sample size was estimated post hoc. Furthermore, they then report the results of the two subgroups (simple fistulas and complex fistulas) rather than the overall results. The numbers in these subgroups are small and although the differences reach statistical significance (operation being significantly better for simple fistulas and fibrin glue being significantly better for complex fistulas) one must be cautious about the conclusions because of the small numbers, that they are based on subgroup analyses, and, finally, there is little biologic rationale why fibrin glue should be more effective in complex than simple fistulas. If the overall results had

been reported, there would have been no statistically significant difference detected.

There are several issues that make surgical trials more difficult to perform including standardization of the procedure and blinding. This trial was performed at one center, increasing the likelihood that the procedure was performed in a similar fashion. But the shortcoming in this trial is that, particularly with complex fistulas, there was no standardized approach to the surgical management. It was left to the discretion of the surgeon whether a fistulotomy would be performed, a seton would be inserted, and, subsequently whether an advancement flap procedure would be performed. With regard to complex fistulas, only 3 patients who had advanced fistulas went on to have a flap advancement procedure. Thirteen were treated with seton alone and one would not expect these to heal. One might predict that the fibrin glue group would do better, although 69% is an impressive healing rate in this difficult group of patients. On the other hand, the authors described in some detail how they prepared the fistula and how they applied the fibrin glue. Although surgeons differ in the details of how they apply fibrin glue, the technique used in this study seems appropriate.

As is the usual patient in surgical trials, the patients and clinicians could not be blinded; an independent assessor could have adjudicated outcomes. The authors fail to mention who assessed outcomes, leaving one to assume that it was the operating surgeon. The primary outcomes was fistula healing as defined as "complete cessation of drainage and the absence of complications." This is quite a subjective outcomes and susceptible to bias in assessing outcomes. The other outcomes of continence, satisfaction, and pain are also subjective and similarly susceptible to bias.

Although there are shortcomings to this trial, the authors are to be congratulated on attempting to study the

use of fibrin glue in a more rigorous way. Complex fistulas, in particular, are difficult because of their heterogeneous nature (i.e.: associated with Crohn's, high, or multiple fistulas) and therefore whereas one would have preferred a more standardized surgical approach, often this is not possible in clinical practice where treatment must be individualized. The fact that these authors showed that fibrin glue seems to be of benefit in above half of patients is a valuable contribution. Many surgeons have not been able to replicate the results of fibrin glue usage in fistulas in the way this has been reported in the literature. This study, too, suffers from a short follow-up of only 12 weeks. Results suggest that perhaps fibrin glue could be tried in patients with complex fistulas as the first line therapy, reserving operation for the failures with the added advantage that there is no compromise of the anal sphincter muscle.

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