

Canadian Association of General Surgeons, the American College of Surgeons, the Canadian Society of Colorectal Surgeons and the American Society of Colorectal Surgeons Evidence-Based Reviews in Surgery – Colorectal Surgery

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

The Canadian Association of General Surgeons and the American College of Surgeons jointly sponsor a program entitled “Evidence-Based Reviews in Surgery” (EBRS). The primary objective of this initiative is to help practicing surgeons improve their critical appraisal skills. Evidence-Based Reviews in Surgery has a module covering topics in colorectal surgery. Each academic year, 6 clinical articles are chosen for review and discussion. The articles are selected not only for their clinical relevance to colorectal surgery, but also to cover a spectrum of methodological issues important to surgeons; for example, causation or risk factors for disease, natural history or prognosis of disease, quantifying disease (measurement issues), diagnostic tests and the diagnosis of disease, and the effectiveness of treatment. Both methodological and clinical reviews of the article are performed by experts in the relevant areas and posted on the Evidence-Based Reviews

in Surgery-Colorectal Surgery (EBRS-CRS) website. In addition, a listserv discussion is held where participants can discuss the monthly article. Members of the Canadian Association of General Surgeons (CAGS) and the American College of Surgeons (ACS) can access EBRS-CRS through the Canadian Association of General Surgeons website (www.cags-accg.ca), the American College of Surgeons website (www.facs.org/education/ebrs.html), the Canadian Society of Colon and Rectal Surgeons (CSRCS) website (www.cscr.ca), and the American Society of Colon and Rectal Surgeons (ASCRS) website (www.fascrs.org). All journal articles and reviews are available electronically through the website. Surgeons who participate in the monthly packages can receive 6 CME and/or Maintenance of Certification credits by completing an evaluation and a series of multiple choice questions each month. For further information about EBRS-CRS, readers are directed to the CAGS, ACS, CSRCS, and ASCRS websites or should send an e-mail message to the administrative coordinator, Marg McKenzie, at mmckenzie@mtsinai.on.ca.

In addition to making the reviews available through the CAGS and the ACS websites, a condensed version of the reviews will be published in the *Diseases of the Colon & Rectum*. EBRS is useful in improving your critical appraisal skills and in keeping abreast of new developments in colorectal surgery; and, most importantly, you are able to obtain 6 CME credits each month from anywhere that you have access to a computer. Comments about EBRS may be directed to mmckenzie@mtsinai.on.ca.

SELECTED ARTICLE

Mushaya C, Barlett L, Schulze B, et al. Ligation of intersphincteric fistula tract compared with advancement flap for complex anorectal fistulas requiring initial seton drainage. *Am J Surg*. 2012;204:283–289.

QUESTION: Is the ligation of intersphincteric fistula tract (LIFT) procedure better than the anorectal advancement flap (ARAF) for the treatment of complex anorectal fistulas?

OBJECTIVE: This article aims to compare the effectiveness of the LIFT procedure with ARAF in the management of complex anorectal fistulas.

DESIGN: This study was performed as a randomized controlled trial.

SETTING: This study was conducted at a single regional hospital in Australia.

PATIENTS: Patients were selected who had a complex fistula, which was defined as follows: the tract crossed more than 30% of the external sphincter, the fistula was a recurrence, there were multiple tracts, the fistula was situated anteriorly in a female or there was preexisting incontinence.

RESULTS: Between December 2007 and February 2011, 39 patients were randomly assigned to the LIFT group (25) or to the ARAF group (14). The median operative time was significantly shorter in the LIFT group than in the ARAF group (10.0 vs 42.5, $p < 0.001$). The complication rates (24% vs 21%, $p = 0.85$) were similar. The mean time to return to normal activities was 1 week for LIFT patients vs 2 weeks for ARAF patients ($p = 0.016$). At a mean follow-up of 19 months, the recurrence rate was 8.0% in the LIFT group compared with 7.1% in the ARAF group ($p = 0.667$).

CONCLUSION: The LIFT procedure can be performed safely, and patients return to work earlier. However, larger trials are required to assess its effectiveness in comparison with ARAF in the management of complex fistula-in-ano.

COMMENTARY: Anal fistulas can be challenging to treat. In addition to there being difficulty identifying the internal opening and multiple external openings, traditional fistulotomy can lead to varying degrees of anal incontinence. In 2007, the LIFT procedure was introduced as a sphincter-sparing treatment for the management of complex anal fistulas.² In this procedure, an incision is made in the intersphincteric groove, and the fistula tract is identified, dissected free, ligated and divided.

Mushaya and colleagues³ performed a randomized controlled trial in patients with complex fistulas to compare the LIFT procedure with an ARAF. It is an important question, because surgeons are definitely looking for options to deal with the complex problem of fistula-in-ano and, to date, only results from small case series have been reported. In this trial, fistulas were defined as complex if the tract crossed more than 30% of the external sphincter, the fistula was a recurrence, there were multiple tracts, the fistula was situated anteriorly in a female, or there was preexisting incontinence. Patients with Crohn's disease were excluded. All patients had a seton inserted before the procedure to eliminate sepsis. Over a 4-year period, 39 patients were randomly assigned: 25 in the LIFT group and 14 in the ARAF group based on a 2:1 randomization scheme. The authors report that operative time was short-

er in the LIFT group (10.0 vs 42.5 minutes, $p < 0.0011$), complications were similar (24% vs 21%, $p = 0.855$), and there was no significant difference in recurrence at a mean of 19 months (7% vs 8%, $p = 0.711$).

Although the authors are to be congratulated on performing this trial (which is rarely done to assess anorectal procedures), this study demonstrates the difficulty in conducting a well-designed randomized controlled trial. First, the definition of recurrence is unclear. The following statement is made: "Recurrence occurred through the original tract and remained trans-sphincteric, and was proven by clinical examination and ultrasound scanning." It is not clear if "recurrence" included both persistence of the fistula from the time of surgery as well as recurrence over time after initial healing. Also, the authors do not report if recurrence was assessed at a specified time point—this is important, because the follow-up time for patients undergoing the LIFT procedure was considerably shorter (16.4 months) than the follow-up of patients in the ARAF group (30 months). Had the groups been followed for similar periods of time, the recurrence rate in the LIFT procedure group may have been higher. Finally, with the use of the authors' definition of recurrence, it would seem that a persistent fistula converted to an intersphincteric fistula by surgery would not be considered a recurrence, but this is not entirely clear.

Second, the trial was designed shortly after the description of the LIFT technique was published.² Little was known about the recurrence/persistence rates after a LIFT procedure. In calculating the sample size, the authors estimated a recurrence rate of 5.6% in the LIFT group and 45.6% in the ARAF group. However, a recent systematic review⁴ of studies of varying design (including the current study) reported that the pooled rate of successful healing with the LIFT procedure was only 71% (failure rate was 29%). On the other hand, a recent review of the literature⁵ indicates that the ARAF is considerably more effective than was estimated by the researchers⁵—the average success rate of the technique for fistula due to cryptoglandular disease pooled from 35 studies was 80.8% (failure rate of 19.2%). Of note, success rates reported in the individual studies included in both of these reviews varied widely.

To determine the sample size, the researchers estimated an absolute improvement in the rate of recurrence of 40% with the LIFT procedure; the risk of recurrence was estimated to be 5.6% for the LIFT procedure compared with 45.6% for the advancement flap procedure. This actually corresponds to a 88% relative risk reduction following the LIFT procedure; although not entirely impossible, estimating a benefit of this magnitude does not seem clinically sensible or perhaps ethical because it would imply there is no equipoise. Instead, if the failure rate (19%) for ARAF reported in the systematic review is used, the rate of failure in the LIFT group would have to be 2.3% to demonstrate an 88% relative risk reduction in the failure rate.

This would seem to be an extremely optimistic estimate particularly when one is considering treatment for complex fistula-in-ano! Furthermore, if the recurrence rate for ARAF of 19% is used to calculate the sample size, and one assumes a relative risk reduction with the LIFT procedure of 88% (recurrence rate of 2.3%), the study would need to include 105 patients with a 1:2 randomization scheme to have a power of 80%. At a more realistic relative risk reduction of 40% (LIFT recurrence rate 11.4%), the estimated sample size would be 763 patients.

Third, patients were allocated by opening a sealed opaque envelope. Although this method has been used in the past, there is a risk of allocation bias in that the surgeon could decide whether to include/exclude the patient in the trial by knowing the group to which the patient would be allocated. However, it does not appear that any patients were excluded from the trial.

So, what can we conclude from this study? Can we say that the 2 procedures are equivalent with respect to recurrence rates? With such small numbers, the most the authors can conclude is that they found no difference in recurrence rates between the 2 techniques. Confidence intervals are used to assess precision. Confidence intervals were not reported by the authors, but they can be calculated: the difference in the rates of recurrence is 0.009 (8% vs 7.1%) with 95% CI ranging from -0.24 to +0.19. In other words, based on these data, we can be 95% confident that the true difference between the recurrence rates for the LIFT procedure and ARAF ranges from 24% in favor of the LIFT procedure to 19% in favor of the ARAF. Because the 95% interval includes differences that most surgeons would consider clinically significant, we cannot conclude that this study has ruled out important differences in recurrence between these 2 treatment options.

What can we learn from this study? This study does add to the continually growing literature that the LIFT procedure is a safe and potentially effective procedure. The LIFT procedure is technically easier to perform than an ARAF. Theoretically there should be a lower rate of incontinence. In previous studies (many of which did not formally evaluate incontinence), a 6% disturbance in continence associated with the LIFT⁴ was reported with higher reported incontinence rates for the flap procedure,⁶ presumably because a portion of the internal sphincter is used to create the flap. The pattern of failure in LIFT procedures is also interesting because when it fails, in some instances, the patient is left with an intersphincteric fistula that can be treated with a fistulotomy.⁷ When a flap fails, the resultant internal opening can be quite difficult to deal with. The use of the LIFT does not burn any bridges, and repeat LIFTs can be used as well as other approaches.

In summary, the authors report excellent results in both groups of this study. Are these results likely to be replicated? Probably not. Is the LIFT a promising new technique

that requires further study? Absolutely. More data from a larger multi-institutional randomized controlled trial are required, but, until we have these data, there are several options available for complex fistulas. Surgeons should choose which procedure to perform based on patient factors as well as his/her comfort in performing the procedure. In addition, sphincter function preservation must always be considered and weighed against success when managing fistula-in-ano.

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