

CORRESPONDENCE



Endoscopic versus Surgical Treatment for Chronic Pancreatitis

TO THE EDITOR: Cahen and colleagues (Feb. 15 issue)¹ suggest the superiority of surgical therapy over endoscopic therapy for chronic pancreatitis and pancreatic-duct obstruction. However, the protocol for endoscopic treatment of pancreatitis and in particular the optional dilation of strictures, the frequency of stent replacement (sequential insertion every 3 months to a maximum of three stents), and the resolution of strictures on radiologic studies as the criteria for termination of endoscopic therapy may explain the disappointing rate of pain relief (32%) in the endoscopy group. Protocols that include routine stricture dilation, more frequent stent placements (every 2 months), and prolonged stent placements (median, 23 months) have reported pain relief in 52 to 62% of patients.^{2,3}

The study by Cahen et al. is important, since there are few randomized, controlled studies of treatment for chronic pancreatitis. Perhaps endoscopists should be more aggressive in their approach rather than recommend surgery.

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Dr. Wong reports serving on advisory boards for Boston Scientific. No other potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: The study by Cahen et al. has at least two limitations. First, there was a very high incidence of strictures (84%) in the endoscopy group, and the patients in this group were treat-

ed with transient stenting (median, 27 weeks); this treatment was shown to be poorly effective 10 years ago.¹ Most recent reports suggest that stents might be removed after 2 years or earlier in the case of concomitant multiple stents,² but no report suggests a return to short-term stenting.

Second, the evaluation of clinical success (the average Izbicki pain score during 2 years of follow-up) does not take into account the major difference between endoscopic treatment, which is associated with a high rate of relapses of pain during the first 2 years and improvement thereafter,³ and surgical therapy, for which the recurrence rates are highest after 5 years, with reintervention required between 5.5 and 7.0 years after initial surgery.⁴

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THIS WEEK'S LETTERS

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TO THE EDITOR: Cahen et al. suggest that surgery is the best option for patients with painful chronic pancreatitis requiring interventional therapy. We have shown in a prospective, randomized trial that extracorporeal shock-wave lithotripsy provides complete pain relief at 4 years in 58% of patients; these results are similar to the results of endoscopic treatment but with fewer procedures.¹ Lithotripsy might be the best initial option in selected patients because it is noninvasive, is less expensive, and does not preclude further endoscopic or surgical therapy.

Better results in our trial are probably related to selection of patients. For example, in the study by Cahen et al., 68% of the patients in the endoscopy group had exocrine pancreatic insufficiency, which suggests a mean duration of 10 years since the onset of disease.^{2,3} A long duration of time since the onset of chronic pancreatitis is associated with a poor outcome after endoscopic treatment.⁴ It would also be interesting to know whether patients with strictures of the common bile duct (indicating long-standing disease) or pseudocysts were included in the study.

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1. Dumonceau JM, Costamagna G, Tringali A, et al. Treatment for painful calcified chronic pancreatitis: extracorporeal shock wave lithotripsy versus endoscopic therapy: a randomised controlled trial. *Gut* 2006;56:545-52.
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TO THE EDITOR: Although Cahen et al. have undertaken a study of an important topic, we believe there are considerable flaws that warrant further discussion. First, a 10-French biliary endoprosthesis

without side holes was inserted into the pancreatic duct in each patient who was treated with stents. Furthermore, stents were in place for 3 months before they were exchanged or removed. Previous studies have shown occlusion of pancreatic stents in 50% of patients by 6 weeks.¹ Smith et al. reported morphologic changes in the pancreatic duct in 80% of patients with stents.² These factors must be weighed heavily, since prolonged stenting with large-bore devices may actually inhibit adequate ductal drainage. The standard of care in the United States is stenting of short duration (2 to 4 weeks) with small pancreatic endoprostheses to limit stent-induced ductal changes and stent occlusion. Without this method of practice, patients are unlikely to have diminished pain.

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TO THE EDITOR: The study by Cahen and colleagues compares endoscopic therapy with surgical drainage of the pancreatic duct in patients with large-duct chronic pancreatitis. To apply the evidence from this study to general clinical practice, it is important to understand that the surgical cohort (patients with a dilated main pancreatic duct, without an inflammatory mass in the pancreatic head and without evidence of biliary stricture) constitutes a minority of most cohorts with chronic pancreatitis.¹

Duct drainage by means of lateral pancreaticojejunostomy is feasible only for patients who have ductal dilatation without an inflammatory mass, and in such patients, the disease is typically at a relatively early stage. Endocrine insufficiency, which is a nearly universal accompaniment of end-stage chronic pancreatitis,² was present in only 20% of the surgical group in this study, confirming that the majority had early-stage chronic pancreatitis. Furthermore, approximately 10% of patients with early disease have small-duct disease and are thus also unsuitable candidates for lateral

pancreaticojejunostomy.³ Thus, although this study is invaluable, the findings are applicable only to a minority of European or North American patients with chronic pancreatitis.

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TO THE EDITOR: The randomized, controlled trial by Cahen et al. showed a clear superiority of surgical drainage over endoscopic drainage of the pancreatic duct in symptomatic chronic pancreatitis. Similar long-term results of another randomized, controlled trial have been reported.¹ Therefore, we were surprised by Elta's statement, in the accompanying editorial,² that endoscopic treatment "remains a reasonable treatment option, depending on patient preferences." The problem with this statement is the term "patient preferences." It is of course the patient who ultimately decides how to proceed with treatment. But we as treating physicians have to inform the patient according to the best available evidence, which now clearly favors surgery. The editorial comment opens a back door that will allow recommendation of endoscopy as first-line therapy, despite better evidence. We have waited a long time for solid evidence regarding the best approach to the management of chronic pancreatitis. Now, we have this evidence for a subgroup of patients, and we should not ignore it. Surgical drainage of the pancreatic duct is the first choice for patients with chronic pancreatitis and associated pancreatic-duct obstruction.

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- Dite P, Ruzicka M, Zboril V, Novotny I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy* 2003;35:553-8.
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THE AUTHORS REPLY: We do not agree with Wong and Delhaye and Devière that our protocol for endoscopic treatment was not up to standard (i.e., not aggressive enough). The presumed superiority of long-term stenting was never proved prospectively and is derived from two observational cohort series only.^{1,2} Moreover, in a recent randomized study, an even less invasive treatment protocol than ours (extracorporeal shock-wave lithotripsy only) was shown to be superior to prolonged and aggressive stenting, in terms of both symptom relief and cost-effectiveness.³

We fully agree with Dumonceau that selection of patients is the key to a correct interpretation of the study outcome. Our results provide evidence that in patients with advanced chronic pancreatitis and extensive disease, the outcome of endoscopy is disappointing. Indeed, endoscopy might still play a valuable role if performed early in the course of disease, but this remains to be proved.

In answer to Buscaglia et al., there is a plethora of pancreatic (side-hole) stents. However, it has never been proved that in chronic pancreatitis these stents are superior to stents without side holes.

We do not agree with Siriwardena that our patients had early-stage chronic pancreatitis, because 68% of the patients in the endoscopy group had exocrine insufficiency, which is a feature of more long-lasting disease activity. Presumably, there are substantial regional differences in the predominant morphologic characteristics of symptomatic chronic pancreatitis, but in our practice, small-duct disease is fairly rare.

Delhaye and Devière suggest that the clinical benefits of endoscopic treatment initially may be inferior to surgery but that these benefits may catch up after 2 years of follow-up. This suggestion could only be regarded as a meager consolation to patients, since to date true evidence is lacking. Obviously, we will continue to follow our patients.

Like Kleeff and coworkers, we also were disappointed by the editorialist's comment that endoscopic treatment "remains a reasonable option, depending on patient preferences." If this is to be considered the overall conclusion of our study, why would one bother to perform a randomized trial, and what about the impact of evidence-based medicine? Patient preference is key, but only if patients are provided with accurate information with which to make a deliberate choice.

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THE EDITORIALIST REPLIES: Although the randomized, controlled trial by Cahen et al. did show the clear superiority of surgical drainage over endoscopic therapy for pain associated with chronic pancreatitis, the study was very small — only 39 patients were included. The previous randomized, controlled trial by Dite et al.,¹ which was similar to that of Cahen et al., included 72 patients, and the authors came to a conclusion that was different from that stated by Kleeff and colleagues. In the study by Dite and colleagues, the initial success rate

was similar for surgery and endoscopic treatment, although at the 5-year follow-up, complete absence of pain was more frequent among the surgically treated patients (34%, vs. 15% among the endoscopically treated patients) and the rate of partial relief was similar (52% and 46%). Dite et al. and a recent guideline from the American Society for Gastrointestinal Endoscopy² concluded that endoscopic treatment may be preferred because of its lower degree of invasiveness, with surgery reserved as second-line therapy.

I agree with Kleeff and colleagues that we owe patients a summary of available evidence so that they can make informed choices regarding their treatment options. However, a single, small study does not adequately summarize the evidence.

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Since the publication of her editorial, Dr. Elta reports serving on the advisory council for MGI Pharma. No other potential conflict of interest relevant to this letter was reported.

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Air Pollution and Cardiovascular Events

TO THE EDITOR: In the report by Miller and colleagues on long-term exposure to air pollution and the incidence of cardiovascular events in women (Feb. 1 issue),¹ the authors state that their robust findings (hazard ratio for death from cardiovascular disease, 1.76) cannot be explained by acute effects of particulate matter. Although particulate matter might subtly promote atherosclerosis,² their findings in no way illustrate synergistic, long-term health consequences of exposure beyond acute effects.

The largest portion of the observed cardiovascular morbidity and mortality is due to particulate matter as a “triggering event” within hours to weeks after exposure. Cohort studies¹ relate long-term levels of particulate matter to events but provide no information regarding the time courses over which exposures actually cause outcomes. The differences between the results of time series (relative risk of death from cardiovascular disease approximately 1.01), which can provide similar data on mortality,³ and the results reported by Miller

et al. are primarily likely to be due to underestimation of the true risk by time series, for multiple reasons. Moreover, case–crossover studies⁴ show that the risks within a single hour after exposure are similar in magnitude to those reported by Miller et al., that lowering pollution dramatically reduces mortality within only months,⁵ and that extending exposure lag-times to weeks yields findings similar to those of cohort studies. It is not biologically plausible that long-term exposure would increase mortality by a factor of 76 (or even by a factor of 2) because of cumulative health responses beyond acute effects (hours to weeks in duration).

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