

## EDITORIAL

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# Outcome and Quality of Life in Chronic Pancreatitis

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## Introduction

Chronic pancreatitis (CP) is a progressive inflammatory disorder that causes abdominal pain, various local complications and endocrine-exocrine pancreatic insufficiency.

In Western countries it is correlated with alcohol abuse in about 75% of cases, constituting a disease process with devastating social consequences since the patients can also become opiate dependent.

The evolution of CP is not easy to study secondary to its relative rarity, delay in diagnosis (on the average 1.5 years after the onset of symptoms), and above all, its long course, on the order of decades, with the average age of onset being around 40 years of age. In any case because the evolution of the disease often lasts longer than the involvement of the doctors in the various research projects, many experiences of generations of researchers in a specific referral period are effectively lost.

## Methods of Evaluating Outcome

We can divide the developmental parameters necessary for the evaluation of the outcome of chronic pancreatitis into three periods.

In the first period the description of morbidity and mortality is limited to the surgical

procedures performed [1, 2, 3]. These parameters considered alone are very limited in their ability to evaluate the evolution of a disease, which by definition is chronic. Emblematic of this are cases of major resections with reduced peri-operative morbidity and mortality, but with severe medium and long-term effects on pancreatic function (diabetes, malnutrition), recurrent pain and loss in working days.

In the second period a series of publications have been produced that have repeated the clinical observations in the follow-up period and which are concerned with gain as an indication of good or bad nutrition, subsequent hospitalizations for complications, and the development of diabetes mellitus. Such effort has been much more accurate than the preceding case and has brought a more realistic description of the life of the patients.

The limit of such an approach consists in the strict medical evaluation, without taking into account the perspective of the patients, who have endured the various procedures, sometimes very invasive, and the subsequent changes in them and their lives. This type of evaluation focusing on the point of view of the patient appears more constant, less is taken for granted, but this is also much more difficult to quantify (see Table 1).

## The Questionnaires on “Quality of Life” (QLQ)

The actual method consists of the use of appropriate questionnaires given to patients and which contain questions regarding their daily lives. Various models exist, some are specific to disease, while some can be used more universally, such as SF-36 [4], which is very useful in many countries. Nonetheless, there still is no specific questionnaire for patients with CP, although some studies to evaluate EORTC QLQ-C30 e PAN26 are already being used in pancreatic cancer [5].

On the basis of the responses obtained it is possible to evaluate the ability to work, social adaptation, cognitive factors and emotions that enable us to understand the patient’s perception of his health, that is to say, the degree of satisfaction and the quality of life. Naturally, this is correlated with the severity of symptoms, type of treatment, duration of the disease, pharmacotherapeutics and characteristics of the patients (weight, diet).

## Utility of Information Obtained

The need to have an adequate instrument to measure the outcome and quality of life is currently very urgent because of the plethora of therapeutic options at our disposal; in fact, aside from the traditional surgical procedures to allieve pain, there are a series of new therapeutic techniques such as extra-corporeal lithotripsy [6], endoscopy and thorascopic splanchnicectomy [7, 8]. These must be tested as objectively as possible, not only in terms of efficacy, but also with regard to the clinical and social consequences [9]. Such methods of evaluation should be effective, trustworthy and be easy to employ even for the patient. This new frontier in which the doctor finds himself has an enormous practical relevance. In the future, the evaluation of the efficacy of a procedure may be based on its effects on the quality of life [10, 11, 12 ]. Today, however, there does not exist a method unequivocally accepted by all and the comparison among diverse methods applied by various centers is

**Table 1.** Some publications with evaluation of quality of life in patients with chronic pancreatitis.

Author	Year	Study	Outcome Evaluated
Bloechle <i>et al.</i> [36]	1995	Quality of life after partial resection of the head of the pancreas.	Questionnaire on quality of life with 50 questions.
Buechler <i>et al.</i> [10]	1995	Randomized trial. Comparing duodenal-preserving pancreatic head resection with pylorus-preserving pancreatic head resection	Evaluation of the quality of life with a 6 month follow-up. Considering: recurrent pain, weight gain, professional rehabilitation.
Broome <i>et al.</i> [37]	1996	Three groups: necrosectomy for acute pancreatitis, chronic pancreatitis treated medically and a control group.	Telephone submitted SF-36 [4] to evaluate quality of life.
Evans <i>et al.</i> [24]	1997	Outcomes of patients with chronic pancreatitis treated surgically.	Evaluation of the quality of life based on: perioperative morbidity and mortality, relief of pain, analgesic use, rehabilitation and long-term surgical sequelae.
Izbicki <i>et al.</i> [38]	1998	Comparison of two surgical procedures: wide drainage of the duct and pancreatic resection.	Questionnaire on the quality of life with 50 questions.
Beger <i>et al.</i> [16]	1999	Outcomes considering patients who underwent a duodenal-preserving pancreatic head resection.	Evaluation of social rehabilitation considering: ability to work, evaluation of pain with a point system, and the Karnofsky index.

not easy. Table 1 illustrates several methods used in recent studies of CP to assess outcome.

### **The Future**

One method, officially appraised and universally applied, could resolve the problem of the lack of uniformity in the evaluation of outcome and could create a true revolution in the therapeutic management of these patients in the various phases of the disease if they were to be referred to more specialized centers.

At the end of 1984, Frey reported a need for an improvement in the evaluation of data in the treatment of CP [13]. One recently published article assessing the treatment of patients with pain from CP [14], confirmed the importance of evaluating 3 factors pre and post-operatively: pain, the use of analgesics and the quality of life. Other authors also recommend an alternative assessment of the quality of life supporting the necessity of a standardized and well-evaluated questionnaire [15]. While waiting for this questionnaire (in reality one already exists and is being evaluated), in more recent publications the authors, mainly surgeons, have begun to add a more precise evaluation of the quality of life to the common series of data.

### **Clinical Evolution: What Is Known ?**

The cardinal symptom of CP is abdominal pain. Various pathophysiologic theories have been explored to explain this and there are two principal schools of thought which identify ductal hypertension and terminal nerve damage, respectively, as the etiology of this pain. This has justified the 2 most diffusely used interventions, surgical and endoscopic decompression of the pancreatic duct and operative resection [16].

Clinically, pain can have 2 origins [17]: the first is due to inflammation and this pain can be significant, similar to an attack of acute

pancreatitis, but it is usually present with episodes of milder intensity, of variable duration and alternating with pain free periods. The pain is particularly intense in the initial 6 years from presentation [18]. As time passes the symptoms tend to decrease more in intensity than in incidence, nonetheless, after 10 years about 50% of the patients still suffer from attacks of pain [19, 20]. In our experience after 15 years of follow-up about 25% of the patients still experience pain, but of these, about 75% have less than 1 recurrence of pain per year [21].

The other type is pain due to complications of the disease. Usually, complications such as pseudocysts, obstructive phenomena which block the emptying of the duodenum or biliary tree, have an excellent chance of being treated surgically. Biliary pathology (stenosis and stones) was reviewed in our series of patients and those who underwent surgery on the biliary tree with or without associated surgery, [390 (46%) subjects], pancreatic pseudocysts developed within 10 years from the onset of symptoms in about 50% of the patients [18] necessitating mainly drainage procedures (pseudocystojejunostomy) though some resections were required.

An important cause of pain is due to obstruction of the duct of Wirsung due to either stenosis or calcification, which develop after 15 years of disease in about 80% of patients.

Peptic pathology is also frequent and 40% of our patients suffer from it during their lifetimes with 14% needing gastric resections, however the majority of these cases were from the pre-H<sub>2</sub>-antagonist era.

### **Late Phase of Chronic Pancreatitis**

The late phase of CP is characterized by exocrine and endocrine pancreatic insufficiency with the presentation of malabsorption and diabetes mellitus. In our series non-insulin dependent diabetes mellitus (NIDDM) was

diagnosed in 45 patients (17%), and insulin dependent diabetes mellitus (IDDM) in 156 (18%), while in 52 cases (6%) both were diagnosed. In 14 patients with IDDM (2%) and in 16 (2%) with NIDDM, the diagnosis of diabetes preceded the presentation of CP.

In a recently published paper IDDM and its complications were shown to have a very negative impact on the quality of life for patients with CP [22], more than many other events thus necessitating frequent follow-up or admissions.

### **What is Obtained Surgically?**

Traditionally, the effective treatment for pain of pancreatic origin can be correctly defined as the primary objective to be achieved. Surgery, resection or drainage, has an important role in treating patients with pain, achieving a lasting resolution in about 70% of cases [16, 18, 23, 24]. After 15 years of follow-up about 70% of the patients undergo pancreatic surgery. In our series 71% of the subjects who underwent a pancreatic jejunal anastomosis for pain no longer suffered from abdominal pain 5 years after the procedure [18].

The mortality in patients with CP varies in 4 studies with similar periods of observation (6.3 to 10 years) from 20.8% to 35% [19, 20, 25, 26]. In our series of 715 patients, the mortality was 25.7% 15 years after the initial presentation of the disease and 37% after 20 years [21]. The principle cause of death is due to extraintestinal malignancies (mainly pulmonary) followed by hepatic cirrhosis (13%), cardiovascular pathology (11%), pancreatic cancer (8%), diabetes mellitus (5%), gastro-intestinal hemorrhage (4%) and acute pancreatitis (2%).

### **Risk of Neoplasia**

One of the most severe late complications is the development of a neoplasm which occurs in about 24% of patients 20 years after the initial presentation of disease [26]. One of the risk factors that seems to be more important in the

pathogenesis of CP than was initially thought is tobacco use [27, 28]. This seems relevant as an independent risk factor for the development of CP [29], but also as a risk factor for pancreatic tumorigenesis [26]. Aside from alcohol, various studies have confirmed the causal association of cigarette smoking and CP [27, 28, 30, 31]. In our group about 700 patients with CP (90%) smoked while in the control population only 35% smoked. This percentage is elevated not only in alcohol related pancreatitis, but also in idiopathic (60% smokers) and familial cases. This association, moreover, of alcohol and tobacco use is in 80% of chronic pancreatitis, yet in only 16% of a population controlled for sex and age [32]. Even though there has been a progressive reduction in the population, the prevalence of smoking in CP has remained elevated and stable in the last 20 years [31].

These habits weigh heavily on the outcome of CP, in fact, at 20 years from presentation about 4% of the patients develop a pancreatic neoplasm [26, 33] while 20% develop an extra-intestinal tumor [26]. These values are notably more elevated than expected upon comparison with data from tumor registries, 13 times more elevated for the pancreatic neoplasms and about 2 times more elevated for other neoplasms.

### **Smokers and Non-Smokers**

In our study we observed that non-smokers with CP had a lower or equal risk of neoplasia than the general population. It was recently calculated that of all pancreatic neoplasms which develop in chronic pancreatitis, about 1/3 are directly due to smoking cigarettes, while the remaining 2/3 are due to smoking and/or other factors [31].

### **Possible Prevention**

In the general population quitting smoking reduces the risk of contracting pancreatic cancer [34]. In our series of CP, excluding the cases that developed after the diagnosis of CP (probably error in diagnosis) [35], none of the

81 non-smokers or of the 82 patients who quit smoking after the presentation of CP have until now developed a pancreatic neoplasm even though the median follow-up is about 12 years [26, 31]. As a result, it is extremely important to suggest that patients with CP stop smoking because this agent is not only a risk factor for the development of the disease and also for the amount of attacks per year [18], but also because it is associated with the development of pancreatic cancer.

### Conclusions

In CP, the initial years after presentation are characterized by pain and the appearance of complications, such as pseudocysts, which profoundly hinder the quality of life of patients. Coupled with a decrease in alcohol intake, there is a confirmed amelioration of pain and treatment of complications after surgery in about 70% of the patients. In the later years of the disease, exocrine pancreatic insufficiency appears (usually discreetly managed with oral supplements), as does diabetes mellitus, which if insulin dependent has a very negative impact on the quality of life. Neoplastic degeneration, often associated with smoking, seems to occur in the last period.

Although not yet adequately quantified, quitting smoking can reasonably be felt to have an important impact on prevention.

The assessment of the quality of life in CP may modify our approach to the treatment of these patients.

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**Key words** Cause of Death; Diabetes Mellitus; Fatal Outcome; Pancreatitis; Pancreatic Neoplasms; Pancreatic Pseudocyst; Quality of Life; Review Literature; Risk Factors; Surgery

**Abbreviations** CP: chronic pancreatitis; IDDM insulin dependent diabetes mellitus;

NIDDM: non-insulin dependent diabetes mellitus; QLQ: questionnaire on Quality of Life

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