# The aetiology of acute and chronic pancreatitis over time in a hospital in Copenhagen

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# ABSTRACT

**INTRODUCTION:** The change in aetiology over time of acute and chronic pancreatitis has been sparsely described, as has also the validity of the diagnostic codes. The aim of the study was 1) to clarify whether the aetiology of acute and chronic pancreatitis changed during the period 1983-2005, and 2) to validate the diagnostic codes over time for acute and chronic pancreatitis registered in the Danish National Patient Registry (NPR) in the same period.

MATERIAL AND METHODS: All admissions at Hvidovre Hospital coded in the NPR in 1983, 1994 and 2005 with a diagnosis of either acute or chronic pancreatitis were included. After exclusion of readmissions, the cohorts consisted of 92, 146 and 118 patients, respectively. Medical records from every admission were retrieved, the aetiology was assessed and the coding of the diagnoses was related to internationally approved criteria.

**RESULTS AND CONCLUSION:** Gallstone disease significantly (p = 0.04) increased as the cause of acute pancreatitis over the 22-year period, while alcohol remained the major cause of chronic pancreatitis. The validity of the diagnoses for patients with acute pancreatitis varied between 51% and 73%, and for chronic pancreatitis between 63 and 78%.

Biliary stones and alcohol are common causes of acute pancreatitis. In accordance with Opie's hypothesis (1901), the cause of gallstone-related acute pancreatitis is thought to be an impacted gallstone in the ampulla of Vater obstructing the pancreatic duct. The mechanisms of alcoholic pancreatitis are unclear, but alcohol may have undesirable effects on the sphincter of Oddi, may change the composition of the pancreatic juice and may directly damage acinar cells. Acute exposition to alcohol leads to acute inflammation, while continuous exposition leads to development of chronic inflammation and fibrosis. In chronic pancreatitis, tobacco also seems to be an important risk factor. However, the aetiology of both acute and chronic pancreatitis remains largely unknown [1-5].

Although both diseases and their complications constitute a burden to public health services, the natural course of the diseases remains sparsely investigated. Epidemiological research within these fields is therefore needed. The Danish National Patient Registry (NPR) is a central registry that collects and stores diagnostic codes for patients admitted to Danish hospitals. Since 1977, all admitted patients have been registered in the NPR with their personal identification number and diagnostic codes. The registry affords a unique opportunity for complete follow-up of a selected cohort and is therefore used extensively for epidemiological research. It is well-known that administrative data from the NPR enjoy a high validity, whereas clinical data such as diagnostic codes given at discharge do not enjoy the same level of reliability [6, 7].

Data on changes in the aetiology of acute and chronic pancreatitis over time are sparse, and little data exist on for the validity of the diagnostic codes in the NPR of both acute and chronic pancreatitis. The primary aim of this study was to clarify whether the aetiology of acute and chronic pancreatitis in our referral population changed during the period 1983-2005. A secondary aim was to validate the diagnostic codes of acute and chronic pancreatitis registered in the NPR in the same period and in the same population.

#### MATERIAL AND METHODS

The study included all admissions to Hvidovre Hospital in 1983, 1994 and 2005 coded with diagnoses of acute or chronic pancreatitis. Most patients were admitted to the departments of surgical and medical gastroenterology, only a few to the paediatric department. The total number of admissions was 513. In 1983, the catchment population counted approximately 133,000 inhabitants, and in 1994 and 2005 approximately 183,000 inhabitants.

### The 1983 cohort

A total of 117 patients were admitted with a diagnosis of either acute or chronic pancreatitis (**Figure 1A**). After exclusion of 25 readmissions, the cohort consisted of 92 patients; 27 with acute pancreatitis and 65 with chronic pancreatitis. The medical record was missing in one case (from the chronic pancreatitis group).

### The 1994 cohort

A total of 210 patients were admitted with a diagnosis of either acute or chronic pancreatitis (Figure 1B). After

#### **ORIGINAL ARTICLE**

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Dan Med Bull 2010;57:A4103 FIGURE 1



exclusion of 64 readmissions, the cohort consisted of 146 patients; 77 with acute pancreatitis and 69 with chronic pancreatitis. Medical records were missing in four cases (equally distributed in the acute and chronic group) and miscoded in nine (6.2%) – four acute and five chronic cases.



Endoscopic retrograde cholangio-pancreaticography showing multiple stones in the gallbladder and stones in the ampulla of Vater in a patient with acute pancreatitis.



# The 2005 cohort

A total of 186 persons were admitted with a diagnosis of either acute or chronic pancreatitis (**Figure 1C**). After exclusion of 68 readmissions, the cohort consisted of 118 patients; 63 with acute pancreatitis and 55 with chronic pancreatitis. A medical record was missing in one case (from the chronic pancreatitis group) and none were miscoded.

Registration of aetiology and validation of the diagnostic codes for acute and chronic pancreatitis was performed retrospectively by review of the original medical records from patients admitted to our hospital in 1983, 1995 and 2005.

For gallstone to be registered as the cause of pancreatitis required findings of stones in the biliary system either by abdominal ultrasound scanning (US), cholecystography, cholangiography, computed tomography (CT), magnetic resonance cholangio-pancreaticography (MRCP), endoscopic retrograde cholangio-pancreaticography (ERCP) or surgery (Figure 2). The notification "possibly biliary" was applied in cases with unverified suspicion of gallstones, e.g. when: 1) the clinical picture was consistent with gallstone but US was unable to visualise stones or was not performed, 2) the radiological findings were uncertain, or 3) ERCP raised suspicion of a passed stone. For alcohol to be registered as the cause of pancreatitis required that the patient had a high consumption of alcohol (> 50 g alcohol per day) up to the admission and that no other aetiology could be demonstrated. The notification "possibly alcoholic" included patients with pancreatitis in whom alcohol was recorded by the discharging doctor as the most probable cause.

In 1983 the diagnoses were coded according to

the WHO's International Classification of Diseases, 8th Edition (ICD8), whereas in 1994 and 2005 the diagnoses were coded according to the WHO's International Classification of Diseases, 10th Edition (ICD10) (**Table 1**). Medical records for every patient were analysed to ascertain that internationally approved diagnostic criteria were met (**Table 2**) [8-14]. The coding was defined as "miscoded" if the admission was coded as pancreatitis and retrospective analysis of the patient record showed that the patient had another disease, e.g. pneumonia, and no signs of pancreatitis.

# STATISTICS

 $\chi^2$  test was used to compare the frequency of acute and chronic pancreatitis of the three years. The level of significance was set at 5% (p < 0.05).

#### RESULTS

### Aetiology

The aetiology of acute and chronic pancreatitis in patients with a valid diagnosis is shown in **Table 3**. Biliary-induced acute pancreatitis was registered as the cause in 5.5% (1/18) of the patients in 1983, 20.0% (11/55) in 1994 and 34.3% (11/32) in 2005. When the category "possibly biliary" was included, the percentages of patients in the respective years were: 5.5% (1/18), 29.0% (16/55) and 44.0% (14/32). Occurrence of alcoholic acute pancreatitis, however, decreased from 61.1% (11/18) in 1983 to 36.4% (20/55) in 1994 and 25.0% (8/32) in 2005. When the category "possibly

# TABLE 1

Diagnostic codes for acute and chronic pancreatitis - before and after 1994.

	ICD8		ICD10		
	codes	used up to and including 31 December 1993	codes	used as from 1 January 1994	
Acute pancreatitis	577.00	Pancreatitis acuta non-haemorrhagica	K.85.9	Pancreatitis acuta	
	577.01	Pancreatitis acuta haemorrhagica			
	577.02	Necrosis acuta pancreatic			
	577.03	Abscessus pancreatic			
	577.04	Pancreatitis non specificata			
	577.08	Pancreatitis acuta alia definita			
	577.09	Pancreatitis acuta			
Chronic pancreatitis	577.19	Pancreatitis chronica, recidivans	K86.0	Pancreatitis chronica alcoholica	
	577.90	Calculus pancreatic	K86.1	Other forms of chronic pancreatitis	
	577.91	Cystis pancreatic	K86.2	Cystis pancreatic	
	577.92	Morbus pancreatis alius	K86.3	Pseudocystis pancreatic	
			K86.8	Other specified pancreatic diseases	
			K86.9	Non-specified pancreatic diseases	

alcoholic" was included, the percentages were: 66.7% (12/18) in 1983, 49.1% (27/55) in 1994 and 28.1% (9/32) in 2005. These changes in the cause of acute pancreatitis over time were significant ( $\chi^2$  test, p = 0.04). Alcohol was the most frequent cause of chronic pancreatitis in 52.0% (26/50) in 1983, 31.0% (13/42) in 1994 and 59.0%

Diagnostic criteria.			Score ≥ 4 is diagnostic [13, 14]		
	Before 1994 [8-11]	After 1994 [12]	symptoms	points	
Acute pancreatitis	Acute abdominal pain + serum amylases/ lipases 2 times upper normal limit (> 600 U/I)	Acute abdominal pain + serum amylases/ lipases 3 times upper normal limit (> 900 U/l)			
or	Typical clinic + amylase > 300 U/l + radiological imaging consistent with acute pancreatitis	Typical clinic + amylase > 300 U/l + radiological imaging consistent with acute pancreatitis			
or	Histological findings consistent with acute pancreatitis (at surgery or postmortem)	Anatomical findings consistent with acute pancreatitis (at surgery or postmortem)			
Chronic pancreatitis			Pancreatic calcifications at x-ray		
			Certain	4	
			Likely	2	
			Histology		
			Certain	4	
			Likely	2	
			Exocrine insufficiency (lipase output < 77 kU/t or fat in stool > 7 g per day)	2	
			Pancreatic duct abnormalities at ERCP	3	
			Loss of weight > 10 kg per 12 months or upper abdominal pain or acute attack of acute pancreatitis	2	
			Diabetes (fasting glucose > 140 mg/dl)	1	
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ERCP = endoscopic retrograde cholangio-pancreaticography.

## TABLE 3

Aetiology of acute and chronic pancreatitis in patients with a valid diagnosis. Numbers (percentage).

ancreatitis	Year	Alcoholic	Possibly alcoholic	Biliary	Possibly biliary	PEP	Others (pancreas divisum, c. pancreatis)	Unknown	All
Acute	1983	11 (61.1)	1 (5.5)	1 (5.5)				5 (27.8)	18 (100)
	1994	20 (36.4)	7 (12.7)	11 (20.0)	5 (9.1)	4 (7.2)	1 (1.8)	7 (12.7)	55 (100)
	2005	8 (25.0)	1 (3.1)	11 (34.4)	3 (9.4)		1 (3.1)	8 (25.0)	32 (100)
Chronic	1983	26 (52.0)	8 (16.0)				1 (2.0)	15 (30.0)	50 (100)
	1994	13 (31.0)	9 (21.4)		1 (2.4)		1 (2.4)	18 (42.9)	42 (100)
	2005	24 (58.5)	4 (9.8)	1 (2.4)	1 (2.4)			11 (26.8)	41 (100)

PEP = post-endoscopic retrograde cholangio-pancreaticography pancreatitis.

(24/41) in 2005. When the category "possibly alcoholic" was included, the percentages of the respective years were: 68.0% (34/50), 52.0% (22/42) and 68.0% (28/41). These changes in the cause of chronic pancreatitis over time were non-significant ( $\chi^2$  test, p = 0.22).

#### Validity

Acute pancreatitis: The diagnostic codes for patients admitted with acute pancreatitis fulfilled current international diagnostic criteria in 66.7% (18/27) of the cases in 1983, 73.3% (55/75) in 1994 and 50.8% (32/63) in 2005 (Figures 1A, 1B & 1C). Of these percentages, 0% were miscoded in 1983, 5.3% (4/75) in 1994 and 0% in 2005.

*Chronic pancreatitis:* The diagnostic codes for patients admitted with chronic pancreatitis fulfilled international diagnostic criteria in 78.1% (50/64) in 1983, 62.7% (42/67) in 1994 and 75.9% (41/54) in 2005 (Figures 1a, 1b & 1c). Of these percentages, 0% were miscoded in 1983, 7.4% (5/67) in 1994 and 0% in 2005.

#### DISCUSSION

This study showed that the registered cause of acute pancreatitis definitely changed over time and that the validity of the diagnostic codes of the NPR for acute and chronic pancreatitis vary.

Gallstones are now the most frequent cause of acute pancreatitis in contrast to three decades ago where alcohol was the most frequent cause. While former studies in Germany and Sweden described a shift from biliary-induced acute pancreatitis to alcoholic acute pancreatitis [5], the present study shows the opposite trend. At Hvidovre hospital, the frequency of biliary-induced acute pancreatitis has risen six-fold, whereas the frequency of alcoholic acute pancreatitis has decreased by 50%. This finding is supported by recent publications [4, 5, 15] from Sweden, Norway, Germany and Denmark. The reason for this shift over time is unclear; however, the increased use of more sensitive diagnostic radiological tools for the diagnosis of gallstones (US, CT, MRCP) during the past three decades has probably contributed to the increase in

gallstones as a major, registered cause of acute pancreatitis. Other reasons may be that there are now fewer heavy consumers of alcohol, more focus on gallstoneinduced pancreatitis and less focus on alcohol-induced disease, and a real increase that may be rooted in a rise in luxurious living. Alcohol remains the most frequent cause of chronic pancreatitis. Several epidemiological studies have revealed a connection between smoking and chronic pancreatitis [1], but it was not possible in this study to extract sufficient and valid information on smoking habits from the medical records to explore such an association.

Because of the outspoken variation in their clinical and biochemical presentation, it may be difficult to diagnose acute and chronic pancreatitis. "The gold standard" is histology, which is rarely available. Several international symposiums have therefore been held within the past three decades with a view to establishing uniform diagnostic criteria for acute and chronic pancreatitis [8-12, 16, 17]. For acute pancreatitis, the diagnostic levels of the serum concentration of amylase or lipase have been raised from two times the upper normal limit to three times the upper normal limit [8-12, 16, 17]. In 1984, the Cambridge symposium [10, 11] facilitated the use of imaging modalities and per-operative findings as supplementary bases for the diagnosis (Table 2), whereas the Marseille criteria for chronic pancreatitis from 1963 were exclusively based on histopathology [16]. The later international symposiums in 1983, 1984 and 1988 added macro-morphological changes demonstrated by diagnostic imaging (US, CT, ERCP) and pancreatic function tests as diagnostic criteria, but the classification system remained of limited practical use [10, 11, 17, 18]. In the present study, the diagnosis of chronic pancreatitis was therefore based on a clinical scoring system described in 1994 by Peter Layer et al from the Mayo Clinic [13] (Table 2).

The non-valid diagnostic codes of acute pancreatitis in this study were primarily due to amylase values below the diagnostic level. Only few were diagnosed on radiological findings combined with insufficient amylase values. Whether the amylase value is the best diagnostic criteria of acute pancreatitis is not to be determined by the present article, but it is, indeed, questionable [19]. For chronic pancreatitis, the non-valid diagnostic codes were either due to miscoding of acute pancreatitis as chronic pancreatitis; or by a lack of findings of either exocrine pancreatic insufficiency, pancreatic calcifications or ERCP changes in patients with abdominal pain, previous acute pancreatitis or previous pancreatic cysts.

Pancreatic cysts, pseudocysts and abscesses are complications to both acute and chronic pancreatitis, but the ICD coding of these diagnoses (*ICD-8: 577.91*, *577.03* and *ICD10: K86.2, K86.3*) pools all these diagnoses as chronic pancreatitis. This leads to an incorrect registration when the complication was actually a consequence of acute pancreatitis. In this material, six patients were coded as chronic pancreatitis complicated by pseudocysts or abscess. Half of these turned out to be complications to acute pancreatitis, and the patients were thus misclassified, which causes a loss of validity.

Epidemiological research is often based on diagnostic registries. The quality of the data of such registries depends on the diagnostic coding made by the clinician at discharge or when filling in the death certificate. Previous studies of the validity of the diagnostic codes in the NPR have shown much variability. Thus, 83% of the diagnoses of orthopaedic patients are correctly registered in the NPR, while this is only the case for about 65% of the codes of medical patients [6, 7]. Floyd et al [5] found a validity of acute pancreatitis diagnosis in the NPR of 82%, whereas this study showed that on average 64% of the diagnoses of acute pancreatitis were correct and 72% of the diagnoses of chronic pancreatitis were correct. Up to 10% of the incorrect diagnostic codes may be ascribed to human or mechanical registration errors [6], which is also in agreement with the finding of 0-6% miscodings in this study. It should also be taken into account that patients with acute or chronic pancreatitis may have been registered with an incorrect diagnostic code and therefore have been wrongly registered in the NPR. The actual amount of false negative diagnoses is therefore unknown. These validity problems can only be avoided by manually revising all hospitalizations at the hospital for all three investigated years, which has not been possible; false positive findings and the possible false negative diagnoses should therefore be taken into account when interpreting research based exclusively on registry data. These problems with the validity of the diagnosis registered in the NPR should be weighed against the unique possibilities of the NPR for tracing individuals over many years. Combined with the completeness of registration, data from the NPR ensures

complete follow-up and minimizes selection bias in epidemiological studies.

A retrospective study like the present entails the risk of introducing bias. The material is somewhat limited in size, especially for the early cohort and it is likely to be unequally distributed, because not all patients were systematically investigated and questioned. Readmissions were excluded in an attempt to make the validation of the diagnostic codes more person-specific. Furthermore, the registered aetiology of pancreatitis depended on individual, subjective interpretation of the course of the admission and the quality of the diagnostic methods over time. The verified aetiology was based on objective findings, but in the "possible" category also on subjective and therefore more biased criteria. Prospective studies are therefore needed to clarify whether the frequency of biliary-induced acute pancreatitis is really increasing.

#### CONCLUSION

An increase in biliary-induced acute pancreatitis over the past two decades was observed, even if alcohol remained the main cause of chronic pancreatitis. The diagnosis of acute and chronic pancreatitis at Hvidovre Hospital was corroborated in 50-78% of cases. The validity of the data should therefore be taken into account when using the NPR for epidemiological research.

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