Acute and chronic pancreatitis: epidemiology and clinical aspects
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Citation for published version (APA):
This thesis focuses on studies concerning acute and chronic pancreatitis, both inflammatory diseases of the pancreas. Two different research areas are presented and therefore this thesis is divided in two parts. Part I contains the epidemiological studies regarding both acute and chronic pancreatitis. Part II concerns studies of different clinical aspects of only acute pancreatitis.

**Part I: Epidemiological studies on acute and chronic pancreatitis**

In [chapter 1] an update is given concerning recent developments in the epidemiology, aetiology, natural course and outcome of acute and chronic pancreatitis. Over the past decades the incidence and the number of hospital admissions in the Western countries for acute and, although less well established, chronic pancreatitis are increasing. These upward time trends seem to relate to a change in the prevalence of the main etiological factors such as gallstones and alcohol consumption. The case-fatality rate of acute pancreatitis decreased over time, but the overall population mortality did not change for acute and chronic pancreatitis.

In [chapter 2] we evaluated the reliability of source data for the National Information System on Hospital Care (NISHC) registry used to classify hospital admissions for both acute and chronic pancreatitis in the Netherlands. All discharge diagnoses related to admissions for acute and chronic pancreatitis in the Academic Medical Center between 2002 and 2003 were re-examined and compared with the data originally notified to the NISHC. We show that there is a substantial miscoding of discharge diagnoses of acute and chronic pancreatitis at the level of individual hospital admissions. However, at a group level, the total numbers of admissions for acute and chronic pancreatitis are only slightly underestimated, 15.8% and 6%, respectively. We conclude that the NISHC may serve as a relatively reliable source for large scale epidemiological studies regarding acute and chronic pancreatitis. In [chapter 3] we used the NISHC registry to describe the trends in hospital admissions in the Netherlands for both acute and chronic pancreatitis in the period 1992 to 2004, and projected the number of admissions up to 2010. In the 12 year time period, both the overall annual number of acute and chronic pancreatitis admissions increased substantially, from 11.8 to 19.2 per 100,000 person-years and, from 5.2 to 8.5 per 100,000 person-years, respectively. The growth rate was higher for women than for men. This trend will most likely continue for the near future. Finally, in [chapter 4] we report the incidence rates of acute and chronic pancreatitis for the period 2000-2005 following linkage of three distinct nation-wide Dutch registries: the NISHC, the population register, and the death certificate register. Also we describe the mortality rates of acute and chronic pancreatitis for the period 1995-2005. Additionally, data on incidence and mortality rates over time are reported for Dutch (year 2000) and international standard populations. We show that between 2000-2005 the incidence of
acute pancreatitis per 100,000 persons per year increased over time for both, males (from 13.8 to 15.2) and females (from 12.7 to 14.2). In contrast to acute pancreatitis, irregular patterns over time emerged for the incidence rates of chronic pancreatitis. The overall mean incidence per 100,000 persons per year was 1.77, for males 2.16, and for females 1.4. Mortality for acute pancreatitis fluctuated during 1995-2005 between 6.9 and 11.7 per million persons per year and was almost similar for males and females. Concerning chronic pancreatitis, the mortality for males fluctuated between 1.1 and 4.0, for females between 0.7 and 2.0. On average, population mortality for both acute and chronic pancreatitis remained fairly stable. Incidence and mortality rates of acute and chronic pancreatitis increased markedly by age and are lower for international standard populations. In light of the continuing ageing of the Dutch population, patient burden and health care costs will most probably increase.

Part II: Clinical aspects of acute pancreatitis

The second part of the thesis starts with an overview of the present literature concerning several aspects of enteral nutrition in acute pancreatitis [chapter 5]. To date, there is substantial scientific evidence that enteral nutrition is preferred over parenteral nutrition in acute pancreatitis. Nasogastric tube feeding appears to be safe and well-tolerated in the majority of patients with severe acute pancreatitis, rendering the concept of pancreatic rest less probable. Enteral nutrition has a beneficial influence on the outcome of acute pancreatitis and should probably be initiated as early as possible (within 48 hours). In [chapter 6] we report an observational study in which the overall nutritional management by attending physician(s) during the time of admission for acute (recurrent) pancreatitis was assessed in a Dutch multicentre setting (EARL study). In this series, the overall nutritional management resulted in a limited total starvation time for both mild and severe acute pancreatitis. It seems that, according to international guidelines, additional nutritional interventions were undertaken early in the course of the disease with enteral feeding via the jejunum as the preferred route. However, physicians should remain vigilant with regard to the nutritional status and nutritional requirements of patients admitted for acute pancreatitis.

In [chapter 7] we evaluated the practice and yield (alternative diagnosis and/or the development of early (peri)pancreatic necrosis) of CT scans acquired within 4 full days after symptom onset in the same cohort of patients with an established clinical diagnosis of acute (recurrent) pancreatitis. We showed that early CT scans are often performed during admission for mild and severe acute pancreatitis. In either group, none of the early CT scans showed pancreatic necrosis, no alternative diagnoses were established, and no relevant implications with regard to clinical management emerged. It seems prudent that clinicians should be more restrictive, especially in mild acute pancreatitis, in the use of early CT scans. An early CT should only be obtained if there is clinical doubt
about the diagnosis of acute pancreatitis or to exclude other life-threatening conditions. Accordingly, unnecessary radiation exposure will be prevented and costs saved.

Finally in [chapter 8] we describe in our observational cohort the use and discontinuation of pancreatitis-associated drugs at hospital admittance and discharge according to a recent evidence-based drug-induced pancreatitis classification system. Drugs are considered a relatively rare cause of acute pancreatitis. We show that pancreatitis-associated drugs are very frequently (70/168 or 41.6%) used at the time of hospital admission for acute (recurrent) pancreatitis. In more than a quarter of cases (44/168 or 26.2%), these pancreatitis-associated drugs are ranked as class I drugs, the highest level of evidence for an association with acute pancreatitis. Physicians must be more aware of the possibility of drug-induced pancreatitis and discontinue pancreatitis-associated drugs at admission accordingly, in particular in recurrent acute pancreatitis of unknown cause.