Dear Sir,

Subcutaneous manifestations of severe acute pancreatitis (Grey-Turner’s sign, Cullen’s sign, Fox’s sign and Walzel’s sign) are often discussed in journals and textbooks. The first two are mentioned even in textbooks ([1]; page 1897). However, despite the publication of several case reports of these skin signs, most physicians have never seen representative cases and therefore do not appreciate the clinical impact of these signs.

Grey-Turner’s sign is produced by spread from the anterior pararenal space between the two leaves of the posterior renal fascia and subsequently to the lateral edge of the quadratus lumborum muscle. Communication may be established to the posterior pararenal space and to the structures of the flank wall. The lumbar triangle, a site of anatomical weakness on the flank wall, may serve as a structural predisposing factor.

Cullen’s sign can be seen following the tracking of liberated pancreatic enzymes to the anterior abdominal wall from the inflamed gastrohepatic ligament and across the falciform ligament. Another more direct pathway may be extension from inflammatory changes of the small mesentery or greater omentum to the round ligament, and from there to properitoneal fat deep to the umbilicus [2].

Fox’s sign is believed to be produced by tracking of the fluid extraperitoneally along the fascia of psoas and iliacus beneath the inguinal ligament until it becomes subcutaneous in the upper thigh [3]. Walzel’s sign, livedo reticularis on the abdomen and/or chest and thighs, is believed to be because of trypsin-induced damage of the subcutaneous venous network [4, 5].

Not all skin signs are specific for acute pancreatitis. Cullen’s sign has been reported in liver biopsy [6] in amoebic liver disease [7], splenic rupture [8], perforated duodenal ulcer [9] and after gynaecological and orthopaedic procedures [10, 11], and may even be artefactual [12]. Fox’s sign may also occur in a ruptured abdominal aortic aneurysm [3].

Ever since their first description, these skin signs have been considered rare and thought to indicate an unfavourable prognosis. Our investigation, the first prospective study of this topic, aimed to establish whether these two assumptions hold true when these signs are actively sought. This report is part of a prospective study on evaluating the severity of acute pancreatitis by means of signs and symptoms as well as prognostic scores. It was conducted in cooperation with the members of the Senior Hospital Gastroenterologists’ Working Group (Arbeitsgemeinschaft Leitender Gastroenterologischer Krankenhausärzte, ALGK).

This study embraces 425 patients in whom the diagnosis of acute pancreatitis was based on the characteristic signs and symptoms, any amylase and/or lipase elevation and abnormal findings on contrast-enhanced computed tomography performed within 96 h after admission and scored according to Balthazar [13]. Parameters for the severity of the disease included arterial pO2, serum creatinine on admission and indications for artificial ventilation and dialysis as well as mortality. All patients were carefully checked for skin signs.

Gender distribution was 53% male ($n = 223$) and 47% female ($n = 197$). The aetiology was biliary disease in 213 patients (50%), alcohol abuse in 126 (30%) and unknown in 30 patients (7%). In 56 patients (13%) other causes were present.

Skin manifestations were found in five patients (1.2%). The Grey-Turner sign alone and the Cullen sign alone occurred in one patient each. Two patients had both of...
these signs and the fifth patient displayed Cullen’s, Grey-Turner’s and Fox’s signs. Four of the five patients were women older than 70 years and had a biliary cause of their disease. The presence of skin signs was significantly associated with renal insufficiency on admission, ventilation, dialysis, severe pancreatitis and mortality as well as necrotizing pancreatitis (Table 1).

The rarity of skin signs in acute pancreatitis in our prospective multicentre study (confined to non-university institutions; see Table 1) correlates well with two reports from university hospitals. Jacobs et al. [14] reported an incidence of skin signs of about 1% in a retrospective analysis of 519 patients and Dickson and Imrie [15] described a rate of 3% in 770 consecutive patients. Remarkably, similar to our findings, the presence of skin signs was not necessarily associated with death in all patients. It is, however, associated with a greatly increased mortality rate compared with all patients with acute pancreatitis. Mortality was 37% [15] and 56% [14]. As in our experience, patients who died were mostly women over 70 years [15].

We conclude that skin manifestations of acute pancreatitis indicate a stormy course of the disease and a poor prognosis. Today the severity of acute pancreatitis is estimated by means of complicated scores and expensive and invasive imaging procedures. Skin signs, if they are looked for, are immediately apparent on physical examination. We hope that this study may serve as a reminder that in acute pancreatitis these skin signs represent a simple and inexpensive parameter for the severity and the prognosis of the disease.

**Conflict of interest statement**

No conflict of interest declared.

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