S3 Guideline for Chronic Pancreatitis – Diagnosis, Classification and Therapy for the Radiologist

S3-Leitlinie Chronische Pankreatitis: Diagnostik, Klassifikation und Therapie für die Radiologie

Abstract

Chronic pancreatitis shows an increasing prevalence and incidence mainly in the Western Hemisphere. Early diagnosis and therapy are frequently delayed because of non-specific symptoms as well as non-specific blood values. The German Society of Digestive and Metabolic Diseases (DGVS) organized the preparation and publication of an interdisciplinary S3 level guideline with the support of the German Radiological Society (DRG) as 1 of 11 contributing societies. In this article we present and discuss the main topics of the guideline regarding the diagnosis, differential diagnosis and therapy of complications of this complex chronic disease with a focus on clinical and scientific radiologists.

Key Points:
- Ultrasound represents the perfect first line imaging modality
- For further diagnostic work up MRI with MRCP are recommended for the differential diagnosis of pancreatic cancer
- For clinical studies the modified (CT, MRI) Cambridge classification is recommended

Introduction

The prevalence and incidence of chronic pancreatitis are increasing in the Western world. The worldwide incidence is between 1.6 and 23 per 100 000 with increasing prevalence [1]. Despite the fact that the disease is typically treated on an outpatient basis, over 10 000 inpatient cases per year have been seen in Germany not including the over 50 000 cases per year of acute episodes of chronic pancreatitis, which are classified as acute pancreatitis. The overall mortality rate of the disease is specified as approximately 28 – 35 % with the death rate of the disease being 3.6 times higher compared to the normal population [2 – 4]. Continued alcohol consumption significantly shortens the survival time for the disease. In the case of alcohol abstinence, the 10-year survival rate is approximately 70 % and the 20-year survival rate is 45 % [5].

Alcohol is the most important risk factor among adults. However, the relationship to alcohol consumption does not appear to be linear [6]. There is no clear indication that chronic pancreatitis is triggered by cholecystolithiasis or choledocholithiasis [7]. Anato-
nostic methods are to be used in a complementary manner. Pain, clinical as well as morphological and functional diag-nostics, which primarily consist of non-specific abdominal functional parameters of the disease. Since these three complications and symptoms are malnutrition and pain vascular or biliary tract complications. The main clinical creatic function and typical complications such as pseu-connective tissue as a result of recurring inflammatory epi-

Definition of chronic pancreatitis

Chronic pancreatitis is defined as a disease of the pancreas in which the pancreatic parenchyma is replaced by fibrotic connective tissue as a result of recurring inflammatory epi-sodes. This results in a loss of exocrine and endocrine pancreatic function and typical complications such as pseudocysts, pancreatic duct stenoses, duodenal stenoses, or vascular or biliary tract complications. The main clinical complications and symptoms are malnutrition and pain syndromes [9]. In addition, the risk of a pancreatic carcino-

Diagnosis of the disease

The guidelines recommend transabdominal sonographic examination of the pancreas as the primary imaging meth-

Table 1 | Sensitivity and specificity of imaging methods for diagnosing chronic pancreatitis according to the current literature.

<table>
<thead>
<tr>
<th>examination</th>
<th>sensitivity</th>
<th>specificity</th>
<th>evidence</th>
<th>references</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>n/a</td>
<td>n/a</td>
<td>2b</td>
<td>[15]</td>
</tr>
<tr>
<td>ERCP</td>
<td>70 – 80 %</td>
<td>80 – 100 %</td>
<td>2a</td>
<td>[14, 15, 47 – 50]</td>
</tr>
<tr>
<td>MRCP</td>
<td>88 %</td>
<td>98 %</td>
<td>2b</td>
<td>[16, 28]</td>
</tr>
<tr>
<td>US</td>
<td>60 – 81 %</td>
<td>70 – 97 %</td>
<td>2a</td>
<td>[14, 26, 51]</td>
</tr>
<tr>
<td>EUS</td>
<td>80 – 100 %</td>
<td>80 – 100 %</td>
<td>2a</td>
<td>[23, 24, 48, 52, 53]</td>
</tr>
</tbody>
</table>


in terms of surgical planning or the differential diagnosis of tumors [15, 26].

**Imaging classification**

Modifications of the Cambridge classification, which was primarily created for ERC, CT, and ultrasound, should be used to classify chronic pancreatitis with imaging methods (Table 2) [27]. In the case of ERC, a classification of Cambridge 0 indicates absolutely no pathological change of the pancreatic duct, Cambridge I indicates less than 3 pathological side branches with a normal main duct, Cambridge II indicates more than 3 pathological side branches with a normal main duct, and Cambridge III indicates more than 3 pathological side branches with a pathological main duct. Cambridge IV additionally includes cystic changes and duct stones and strictures. As mentioned above, the original Cambridge classification was limited to duct visualization via ERP with an expansion to include CT and ultrasound.

Therefore, adaptations and standardizations of the nomenclature for sonography, CT and primarily MRCP are being undertaken and will be important for future multimodal clinical studies [12, 18, 28–30]. In the radiological adaptation of the Cambridge classification (Fig. 1–3) for CT and MRI, the modification of Cambridge 0 entails absolutely no changes. Changes cannot be defined in Cambridge 1 with current CT and MRI techniques. In the CT/MRCP modification, Cambridge 2 means 2 or more of the following changes (Fig. 1): Pancreatic duct between 2 mm and 4 mm in the body of the pancreas, discrete enlargement of the pancreas, heterogeneous parenchymal structures, cystic changes < 10 mm, duct irregularities, pathological side ducts. In the case of Cambridge 3 (Fig. 2), all of the changes mentioned for II must be present with a pathological main duct, while in Cambridge 4 (Fig. 3) cystic structures > 10 mm with parenchymal calcifications (Fig. 4), interductal defects, duct obstructions, and severe duct irregularities must additionally be present. In contrast to the ERP-based Cambridge classification, changes in the pancreatic parenchyma are

<table>
<thead>
<tr>
<th>Cambridge</th>
<th>ERCP</th>
<th>CT/MRCP</th>
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<tbody>
<tr>
<td>0</td>
<td>no pathological changes with complete visualization of the pancreatic duct</td>
<td>none</td>
</tr>
<tr>
<td>1</td>
<td>fewer than 3 pathological side branches, normal main duct</td>
<td>cannot be delimited in CT/MRCP with current methods</td>
</tr>
<tr>
<td>2</td>
<td>3 or more pathological side branches, normal main duct</td>
<td>2 or more of the following changes:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– pancreatic duct between 2 and 4 mm in the body of the pancreas</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– slight enlargement of the pancreas</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– heterogeneous parenchymal structure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– small cystic changes (&lt; 10 mm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– duct irregularities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– 3 or more pathological side ducts</td>
</tr>
<tr>
<td>3</td>
<td>3 or more pathological side branches plus pathological main duct</td>
<td>all changes specified in 2 plus pathological main duct (&gt; 4 mm)</td>
</tr>
<tr>
<td>4</td>
<td>as in 3 plus cysts, duct stones, strictures, involvement of neighboring organs</td>
<td>one of the changes specified in 2 and 3 plus one or more of the following:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– cystic structures &gt; 10 mm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– parenchymal calcifications intraductal filling defects (chalk stones)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– duct obstruction (strictures), severe duct irregularities</td>
</tr>
</tbody>
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**Table 2** Summary of the Cambridge classification with modification for CT and MRCP.

**Fig. 1** 56-year-old patient with chronic pancreatitis (Cambridge 2): a Coronary 3D-MIP-MRCP with discretely dilated pancreatic duct (to 3 mm) with duct irregularities and small, cystic changes. b Corresponding axial T2 se-

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also taken into consideration in the imaging methods. In principle, this classification should be primarily used for study classification since it provides a uniform classification even for different imaging methods.

**Imaging of typical complications of chronic pancreatitis**

In the case of necrosis, contrast-enhanced ultrasound examination (CEUS) is put on par with contrast-enhanced CT even though an evaluation of severity as in CT is not possible [31]. Moreover, this statement is based on a single publication and has not yet been confirmed by further studies [32]. In the clinical routine contrast-enhanced CT continues to be the method of choice due to its high availability and objectivity especially since CEUS currently still requires a high degree of specialization on the part of the examiner. Contrast-enhanced MRI can also be used with the same sensitivity and specificity. However, this still plays a secondary role in practice [32, 33].

In the case of cysts (Fig. 5), transabdominal ultrasound is initially viewed as sufficient. EUS and MRI with MRCP are specified as additional methods for differentiation with a higher transfer rate between pancreatic lesions. However, sonography should typically be sufficient [34].

In the case of vascular changes, pseudoaneurysms in particular are a typical complication. Basic diagnosis via sonography with additional color Doppler is typically sufficient in most cases. For interventional and surgical planning, CT angiography or MR angiography should be performed. However, as in the case of sonography, there are also no adequate comparative studies here.

**Differential diagnosis in chronic pancreatitis**

When diagnosing pancreatic carcinomas in patients with chronic pancreatitis, regular percutaneous ultrasound pro-
vides insufficient differentiation between carcinomas and inflammatory changes. EUS with fine-needle puncture has a sensitivity of over 85% [35, 36]. For MRI with MRCP current studies specify sensitivities of approximately 84% with a specificity of 97%, while a sensitivity of 93% and a specificity of 75% were calculated for the differentiation between focal pancreatic masses in chronic pancreatitis and pancreatic carcinomas [37]. Both necrotic changes and pancreatic carcinomas have hypoperfused areas. Since EUS-based fine-needle puncture has a relatively high rate of false-negative findings, its use for ruling out surgical treatment also seems limited [38]. Histological or cytological fine-needle puncture can be helpful for the differentiation between autoimmune pancreatitis and other pancreatic diseases since up to 40% of cases of autoimmune pancreatitis present with focal lesions [39]. In principle, there is virtually no diagnostic value in performing ERP as a primary diagnostic method. Four criteria with a high sensitivity and specificity were defined only for autoimmune pancreatitis. Long stenoses > 1/3 of the pancreatic length, a lack of dilatation of the downstream pancreatic duct, dilatation of the side branches and multifocal strictures in the course of the pancreatic duct are described as changes indicative of autoimmune pancreatitis [34]. ERP is therefore still required for diagnosing autoimmune pancreatitis in the Japanese guidelines. ERP is explicitly not specified as the primary diagnostic method in the German S3 guideline. Instead, EUS and/or MRI with MRCP is recommended. ERP should only be performed in individual cases of unclear EUS or MRCP findings.

**Vascular complications**

In particular, vascular pseudoaneurysms in chronic pancreatitis must be mentioned here. These should be treated due to a risk of bleeding although there are no evidence-based prospective studies. Bleeding pseudoaneurysms should be treated due to the low morbidity of the radiological-interventional method compared to surgery with angiographic embolization. According to the literature, the success rate of angiography is approximately 66% [42].

**Treatment of typical complications**

Pancreatic pseudocysts are the most common complication of both acute and chronic pancreatitis with the prevalence in chronic pancreatitis being 20–40% [40]. Pancreatic pseudocysts are most common in patients with alcohol-based chronic pancreatitis [2]. Pancreatic pseudocysts spontaneously regress 6 weeks after formation in up to 40% of patients. If pseudocysts persist for more than 12 weeks, spontaneous remission is very improbable with additional complications occurring in up to 60% of cases [41]. The timing and the performing of possible therapeutic interventions in the case of pancreatic pseudocysts were partially controversial in the guideline discussion. According to the published guidelines, pseudocysts with a total size of over 5 cm and a capsule with a thickness of more than 5 mm were associated with complications. Treatment can be in the form of surgery in terms of fenestration or percutaneous and endoscopic drainage. The data regarding intervention in the case of pseudocysts is very limited. There are no suitable prospective studies. Placement of a stent in the bile duct can be sufficient in the case of cholestasis caused by a pseudocyst. In the case of compression of larger vessels or gastric outlet stenoses, the pancreatic pseudocyst should be drained. However, an endoscopic endoluminal drainage procedure that seems to have fewer complications than a surgical approach should be given preference [34, 40]. In principle, percutaneous radiological procedures are possible but are associated with a high risk of external fistula formation so that this method should not be performed if endoscopic drainage is possible. Particularly in the case of infected cysts, drains placed under radiology guidance have worse results than endoscopically placed drains. However, both minimally invasive procedures are better than the surgical approach [40].
Follow-up

Examinations and imaging methods in intervals between 6 and 12 months after diagnosis are recommended for clinical follow-up to detect complications early. However, there are insufficient studies to support this time interval. In addition to clinical and laboratory examinations, follow-up primarily with transabdominal ultrasound examinations is recommended and with a sensitivity of approximately 60 – 81 % is largely in the range of the sensitivity of CT or MRI examinations (Table 1). The only problem with ultrasound examination is poor specificity of approximately 35 % so that the examination should be supplemented by EUS, ERCP, CT, or MRI in the case of unclear findings [43]. In the case of suspicion of a complication or the formation of a pancreatic carcinoma, the corresponding imaging (CT or MRI/MRCP) must be performed in the further course. None of the described methods has sufficient reliability to definitively rule out an operable malignancy in the case of chronic pancreatitis. According to the current literature, endosonography seems to be superior particularly due to the possibility to take biopsies. However, MRI with MRCP can be assigned a higher diagnostic value [14, 36]. Tumor markers are not very helpful with respect to pancreatic carcinomas in patients with chronic pancreatitis. The diagnostic sensitivity and specificity are not sufficient. The extent to which MRI together with diffusion-weighted sequences and dynamic MRI examinations can provide additional differential diagnostic help must be further clarified. Based on the current literature, it seems rather improbable that MRI with diffusion-weighted sequences will result in a relevant improvement in differential diagnosis [44 – 46].

Summary

According to the first evidence-based German S3 guidelines regarding the diagnosis and treatment of chronic pancreatitis, transabdominal sonography is the basic examination of choice for initial diagnosis as well as in the further course for early clarification of possible complications. MRI with MRCP has a very high diagnostic value both for classification for studies and for early diagnosis and differential diagnosis of possible pancreatic carcinomas that frequently occur in patients with chronic pancreatitis. The Cambridge classification should be used in studies since it provides comparable classifications and results via modifications for the most important imaging methods. Transcutaneous methods should only be used on a limited basis in the treatment of complications, such as pancreatic pseudocysts, since fistula formation is a common complication. Angiographic embolization of vascular aneurysms in chronic pancreatitis is the method of choice for acute bleeding or for prophylaxis.

References

7 Yan MX, Li YQ, Gall stones and chronic pancreatitis: the black box in between. Postgraduate medical journal 2006; 82: 254 – 258