Amsterdam UMC

Amsterdam UMC

ESPEN practical guideline on clinical nutrition in acute and chronic pancreatitis

Arvanitakis, Marianna; Ockenga, Johann; Bezmarevic, Mihailo; Gianotti, Luca; Krznarić, Željko; Lobo, Dileep N.; Löser, Christian; Madl, Christian; Meier, Remy; Phillips, Mary; Rasmussen, Henrik H. jgaard; van Hooft, Jeanin E.; Bischoff, Stephan C.

Published in:
Clinical Nutrition

DOI:
10.1016/j.clnu.2023.12.019

Published: 01/02/2024

Document Version
Publisher's PDF, also known as Version of record

Document license
Taverne

Link to publication

Citation for pulished version (APA):
Arvanitakis, M., Ockenga, J., Bezmarevic, M., Gianotti, L., Krznarić, Ž., Lobo, D. N., Löser, C., Madl, C., Meier, R., Phillips, M., Rasmussen, H. H. J., van Hooft, J. E., & Bischoff, S. C. (2024). ESPEN practical guideline on clinical nutrition in acute and chronic pancreatitis. *Clinical Nutrition*, *43*(2), 395-412. https://doi.org/10.1016/j.clnu.2023.12.019

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Amsterdam UMC Medical Library know, stating your reasons. In case of a legitimate complaint, the Medical Library will make the material inaccessible and/or remove it from the website. Contact address: outputregistratie@amsterdamumc.nl

Download date: 09. Oct. 2026

Clinical Nutrition 43 (2024) 395–412

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

ESPEN Guideline

ESPEN practical guideline on clinical nutrition in acute and chronic pancreatitis

Marianna Arvanitakis [a, *], Johann Ockenga [b], Mihailo Bezmarevic [c], Luca Gianotti [d], Željko Krznarić [e], Dileep N. Lobo [f, g, h], Christian Löser [i], Christian Madl [j], Remy Meier [k], Mary Phillips [l], Henrik Højgaard Rasmussen [m], Jeanin E. Van Hooft [n], Stephan C. Bischoff [o]

[a] Department of Gastroenterology, Hepatopancreatology, and Digestive Oncology, HUB Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium
[b] Department of Gastroenterology, Endocrinology and Clinical Nutrition, Klinikum Bremen Mitte, Bremen, Germany
[c] Department of Hepatobiliary and Pancreatic Surgery, Clinic for General Surgery, Military Medical Academy, University of Defense, Belgrade, Serbia
[d] School of Medicine and Surgery, University of Milano-Bicocca and Department of Surgery, San Gerardo Hospital, Monza, Italy
[e] Department of Gastroenterology, Hepatology and Nutrition, Clinical Hospital Centre & School of Medicine, Zagreb, Croatia
[f] Gastrointestinal Surgery, Nottingham Digestive Diseases Centre and National Institute for Health Research Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust and University of Nottingham, School of Medicine, Queen's Medical Centre, Nottingham, NG7 2UH, UK
[g] MRC Versus Arthritis Centre for Musculoskeletal Ageing Research, School of Life Sciences, University of Nottingham, Queen's Medical Centre, Nottingham, NG7 2UH, UK
[h] Department of Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
[i] Medical Clinic, DRK-Kliniken Nordhessen, Kassel, Germany
[j] Division of Gastroenterology and Hepatology, Krankenanstalt Rudolfstiftung, Krankenanstaltenverbund Wien (KAV), Vienna, Austria
[k] AMB-Praxis-MagenDarm Basel, Basel, Switzerland
[l] Department of Nutrition and Dietetics, Royal Surrey County Hospital NHS Foundation Trust, Guildford, UK
[m] Centre for Nutrition and Bowel Disease, Department of Gastroenterology, Aalborg University Hospital, Faculty of Health, Aalborg University, Aalborg, Denmark
[n] Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, the Netherlands
[o] Institute of Nutritional Medicine, University of Hohenheim, Stuttgart, Germany

ARTICLE INFO

Article history:
Received 29 November 2023
Accepted 23 December 2023

Keywords:
Acute pancreatitis
Chronic pancreatitis
Pancreatic diseases
Nutrition
Nutritional support
Medical nutrition

SUMMARY

Both acute and chronic pancreatitis are frequent diseases of the pancreas, which, despite being of benign nature, are related to a significant risk of malnutrition and may require nutritional support. Acute necrotizing pancreatitis is encountered in 20 % of patients with acute pancreatitis, is associated with increased morbidity and mortality, and may require artificial nutrition by enteral or parenteral route, as well as additional endoscopic, radiological or surgical interventions. Chronic pancreatitis represents a chronic inflammation of the pancreatic gland with development of fibrosis. Abdominal pain leading to decreased oral intake, as well as exocrine and endocrine failure are frequent complications of the disease. All of the above represent risk factors related to malnutrition. Therefore, patients with chronic pancreatitis should be considered at risk, screened and supplemented accordingly. Moreover, osteoporosis and increased facture risk should be acknowledged in patients with chronic pancreatitis, and preventive measures should be considered.

© 2023 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.

1. Introduction

Acute pancreatitis (AP) is the most common acute gastrointestinal disease requiring hospital admission [1], with the outcome being favorable in most cases (80 %) [2]. However, acute necrotizing pancreatitis (ANP) may develop in up to 20 % of patients and is associated with significant rates of early organ failure (38 %), need for intervention (38 %), and death (15 %) [2]. Catabolism is very high in this setting; therefore, nutritional support is one of the cornerstones of management [3]. A significant amount of research has shown the superiority of enteral nutrition (EN) over parenteral nutrition (PN) in ANP, creating a paradigm shift a decade ago and modifying the management strategy [3]. Nevertheless, additional questions regarding the timing, route and type of EN, as well as the place of oral refeeding, are still the objects of clinical investigations.

Chronic pancreatitis (CP) is a disease in which recurrent inflammatory episodes lead to replacement of the pancreatic

* Corresponding author.
E-mail address: Marianna.arvanitaki@erasme.ulb.ac.be (M. Arvanitakis).

https://doi.org/10.1016/j.clnu.2023.12.019
0261-5614/© 2023 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.

Abbreviations

ACS	acute compartment Syndrome
ANP	acute necrotizing pancreatitis
AP	acute pancreatitis
BMI	body mass index
CP	chronic pancreatitis
DXA	dual-energy X-ray absorptiometry
EN	enteral nutrition
IAH	intra-abdominal hypertension
IAP	intra-abdominal pressure
MCT	medium chain triglycerides
ONS	oral nutritional supplements
PEI	pancreatic exocrine insufficiency
PERT	pancreatic enzyme replacement therapy
PN	parenteral nutrition
PPI	proton pump inhibitor
RCT	randomized controlled trial
SIBO	small intestinal bacterial overgrowth

parenchyma by fibrous connective tissue [4]. The major consequence of CP is the loss of functional exocrine and endocrine pancreatic tissue, thus resulting in both exocrine and endocrine insufficiency [4]. Pain is also frequently encountered in patients with CP, and seems to be related to a multitude of factors such as pancreatic neural remodeling and neuropathy, increased intraductal and parenchymal pressure, pancreatic ischemia and acute inflammation during an acute relapse [5]. Both pain and loss of pancreatic function can lead to malnutrition in patients with CP [4]. Moreover, other long-term consequences such as osteoporosis are frequently overlooked, despite their potential impact on quality of life in patients with CP. Therefore, screening for malnutrition and nutritional support play a crucial part in the multimodal management required in this setting.

Although recent guidelines for AP [2] and CP [4] have been published, a dedicated consensus on nutritional support in pancreatic diseases is lacking. The recently published guideline from European Society for Clinical Nutrition and Metabolism (ESPEN) provided specific recommendations focused on clinical nutrition for patients with acute or chronic pancreatitis to fulfill the gap [6].

2. Methodology

The present practical guideline consists of 42 recommendations and six statements and is based on the aforementioned ESPEN guideline on clinical nutrition in acute and chronic pancreatitis [6]. The original guideline was shortened by focusing the commentaries on the evidence and literature on which the recommendations are based on. The recommendations were not changed, but the presentation of the content was transformed into a graphical presentation. The original guideline was developed according to the standard operating procedure for ESPEN guidelines and consensus papers [7].

A comprehensive, systematic literature search was performed on 1st December 2018, based on 31 clinical questions in PICO (population of interest, interventions, comparisons, outcomes) format. Existing evidence was graded according to the SIGN (Scottish Intercollegiate Guidelines Network) grading system. Recommendations were developed and graded into four classes (A/B/0/GPP) [7].

All recommendations were agreed in a multistage consensus process, which resulted in a percentage of agreement (%). The guideline process was funded exclusively by the ESPEN society. For further details on methodology, see the full version of the ESPEN guideline [6] and the ESPEN standard operating procedure [7].

3. Acute pancreatitis (Fig. 1)

1) **Patients with acute pancreatitis should be considered at moderate to high nutritional risk, because of the catabolic nature of the disease and because of the impact of the nutritional status for disease development.**

(S1, strong consensus, 97 %)
Commentary

Fortunately, the majority of patients with AP have predicted mild or moderately severe forms of the disease that are self-limited with fully recovery in less than a week, in whom oral feeding can be started within few days after the onset of AP [8]. Gut-barrier dysfunction may occur in up to 60 % of patients with AP; mostly in severe AP and it is thought to lead to bacterial translocation and infection of necrosis [9]. Along with the increased catabolic state related to the disease, patients with predicted severe AP are considered at nutritional risk [10]. Nevertheless, malnourished patients should also be considered at nutritional risk, even if they have predicted mild AP, because of their pre-existing condition. Similarly, patients with increased alcohol consumption are frequently malnourished [11].

3.1. Acute pancreatitis – mild to moderate disease (Fig. 2)

3.1.1. Nutritional screening

2) **All patients with predicted mild to moderate acute pancreatitis should be screened using validated screening methods such as the Nutritional Risk Screening – 2002 (NRS-2002); however, the patients with predicted severe acute pancreatitis should always be considered at nutritional risk.**

(R1, grade B, strong consensus, 100 %)
Commentary

Scoring systems such as the NRS 2002 [12], can be helpful in identifying these patients [13–16]. These scores have been validated in hospitalized, as well as critically ill patients. Nevertheless, no studies have validated these scoring systems in a specific population of patients with AP [17].

A low body mass index (BMI) may also identify patients who are at nutritional risk. Nevertheless, obesity is a known risk factor for severe AP and is, therefore, a disease severity-related nutritional risk [18].

3.1.2. Oral feeding with low fat soft diet

3) **Oral feeding shall be offered as soon as clinically tolerated and independent of serum lipase concentrations in patients with predicted mild AP.**

(R2, grade A, strong consensus, 100 %)
Commentary

Four randomized controlled trials (RCTs) have shown that patients with mild to moderate AP can tolerate early oral feeding and this strategy is related with a shorter length of stay compared with conventional oral feeding (introduced after enzyme decrease,

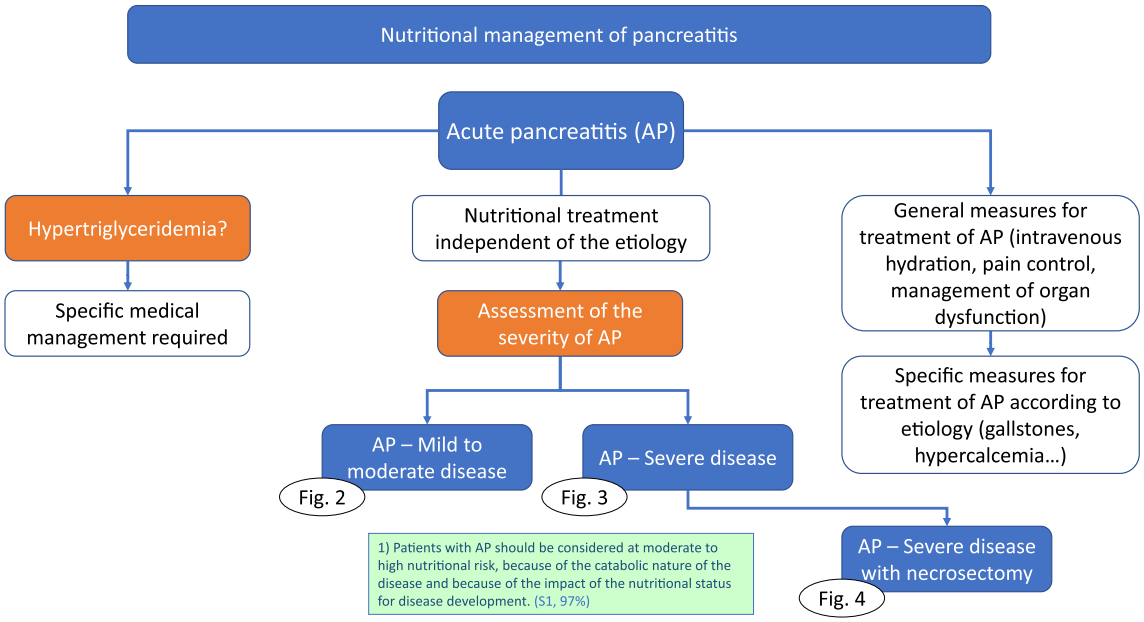

Fig. 1. Nutritional management of acute pancreatitis. AP, acute pancreatitis.

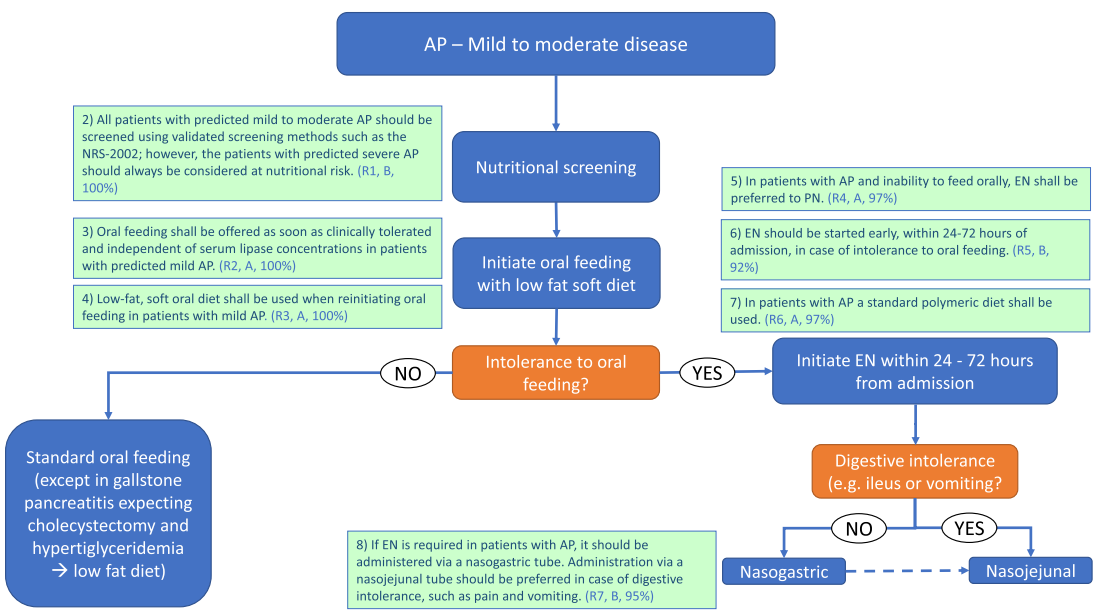

Fig. 2. Management of mild to moderate acute pancreatitis. AP, acute pancreatitis; EN, enteral nutrition; NRS-2002, Nutritional Risk Screening – 2002; PN, parenteral nutrition.

pain resolution and bowel movement) [8,19–22]. Furthermore, one of these trials revealed that oral food intake is safe and well-tolerated independently of the course and normalization of serum lipase [19].

4) **Low-fat, soft oral diet shall be used when reinitiating oral feeding in patients with mild acute pancreatitis.**

(R3, grade A, strong consensus, 100 %)

Commentary

Immediate oral feeding with a soft diet seems to be more beneficial regarding caloric intake and equally tolerated compared with clear liquid diets [22–24]. A meta-analysis confirmed that early oral feeding was feasible in patients with predicted mild AP and reduced length of stay [25]. A recent meta-analysis including 17 studies identified that 16.3 % of patients with AP will subsequently have intolerance to oral feeding [26]. Hyperlipidemia is the third most common cause of AP and accounts for 4–10 % of cases, while it has been reported to be associated with a worse prognosis compared to other etiological factors [27–29]. Specific management includes initially putting patients on a nil by mouth regimen for 24–48 h, followed by subsequent dietary modifications, medical management with the different classes of anti-hyperlipidemic agents, in-hospital

pharmacological treatment with insulin and/or heparin and plasmapheresis [27,28].

3.1.3. Enteral nutrition in case of intolerance to oral feeding

5) **In patients with acute pancreatitis and inability to feed orally, enteral nutrition shall be preferred to parenteral nutrition.**

(R4, grade A, strong consensus, 97 %)
Commentary

EN is supposed to preserve the integrity of the gut mucosa, stimulate intestinal motility, prevent bacterial overgrowth, and increase the splanchnic blood flow [9]. Currently there are twelve RCTs and eleven systematic reviews/meta-analyses including a Cochrane-standard meta-analysis which clearly prove that in patients with severe AP, EN is safe and well-tolerated, with significant decreases in complication rates, multi-organ failure, and mortality, compared with PN [30–40]. The meta-analysis by Al-Omran et al. was performed to Cochrane-standards on the basis of eight RCTs with 348 patients and clearly shows that early EN when compared with initial total PN, significantly decreases mortality by 50 % (OR 0.50 [95 % CI 0.28 to 0.91]), rate of infection (OR 0.39 [95 % CI 0.23 to 0.65]), multi-organ failure (0.55 [95 % CI 0.37 to 0.81]) as well as the necessity for operation (OR 0.44 [95 % CI 0.29 to 0.67]) [34]. Furthermore if only patients with severe AP were included in this meta-analysis, mortality further decreased by more than 80 % [0.18 [95 % CI 0.006 to 0.58]) [34]. These results were confirmed by more recent meta-analyses, including a latest publication including only critically ill patients with AP [38]. Compared with PN, EN was associated with a significant reduction in overall mortality (RR 0.36, 95 % CI 0.20 to 0.65, $p = 0.001$) and the rate of multiple organ failure (RR 0.39, 95 % CI 0.21 to 0.73, $p = 0.003$).

6) **Enteral nutrition should be started early, within 24–72 h of admission, in case of intolerance to oral feeding**

(R5, grade B, strong consensus, 92 %)
Commentary

Several meta-analyses have investigated the clinical effects and tolerance of early EN in patients with AP either within 24 h [41–43] or 48 h [44–46] of admission. All these meta-analyses clearly reveal that early EN is feasible, safe and well-tolerated and associated with substantial clinical benefits regarding mortality, organ failure and infectious complications for both time-points compared with delayed EN. Nevertheless, a potential bias could be that five of these meta-analysis included studies which had patients receiving PN in their control groups [41–45]. One meta-analysis, compared early (within 24 h) with late EN (after 72 h), but no comparison was made between 24 and 48 h [43].

In contrast to these data from the aforementioned meta-analyses that provided strong evidence for early EN within 24–48 h, a multicenter RCT (208 patients with predicted severe AP) found no difference in the rate of major infection or death between early EN, started within 24 h after admission, and an oral diet initiated 72 h after admission [43]. A second RCT (214 patients with AP) confirmed these results [47].

Finally, a prospective cohort study including 105 patients with AP concluded that the third day after hospital admission was the best cut-off time for early EN (with an area under the curve of 0.744), by reducing the risk of secondary infection and improving the nutritional status of patients, with a better tolerance [48].

7) **In patients with acute pancreatitis a standard polymeric diet shall be used.**

(R6, grade A, strong consensus, 97 %)
Commentary

Most studies that evaluated the clinical benefits of early EN in comparison with total PN used semi-elemental formulae while the recent studies were performed with polymeric formulae. In all studies both types of formulae were proven to be feasible, safe and well-tolerated. One small RCT in 30 patients found that both formulae were safe and well-tolerated (based on a visual analogue scale and number of stools per day) with some clinical benefits for semielemental diets, including length of stay (23 ± 2 *vs.* 27 ± 1 days, $p = 0.006$) and weight maintenance [49]. On the other hand an indirect adjusted meta-analysis of Petrov et al. on 428 patients using PN as a reference treatment showed no differences regarding tolerance, rate of infection and mortality between both formulae [50]. Finally, a second, more recent meta-analysis, including 15 trials (1376 participants), showed no evidence to support a specific enteral formula [51]. Nevertheless, a subgroup of patients with severe AP may have malabsorption and therefore, semi-elemental diets could be of interest.

8) **If enteral nutrition is required in patients with acute pancreatitis, it should be administered via a nasogastric tube. Administration via a nasojejunal tube should be preferred in case of digestive intolerance, such as pain and vomiting.**

(R7, grade B, strong consensus, 95 %)
Commentary

Three RCTs compared nasojejunal with nasogastric support route in patients with severe AP [52–54] showed no differences regarding tolerance, complications rates and mortality. Four meta-analyses [55–58] conclude that nasogastric tube feeding is feasible, safe and well-tolerated and, compared with nasojejunal tube feeding, does not increase complication rate, mortality, refeeding pain recurrence or prolong hospital stay in patients with severe AP. Compared with nasojejunal tubes, nasogastric tubes are much easier to place, more convenient and cheaper. Nevertheless, about 15 % of patients will experience digestive intolerance, mostly because of delayed gastric emptying and gastric outlet syndrome [55,56] and in this situation, nasojejunal tube feeding is required. Furthermore, potential bias arises from the small number of patients included in the aforementioned trials and the use of different criteria to define severe AP.

3.2. Acute pancreatitis – severe disease (Fig. 3)

3.2.1. Parenteral nutrition in case of intolerance of enteral nutrition

9) **PN should be administered in patients with acute pancreatitis who do not tolerate enteral nutrition or who are unable to tolerate targeted nutritional requirements, or if contraindications for EN exist.**

(R8, grade GPP, strong consensus, 97 %)
Commentary

The primary nutritional route in all patients with severe AP should be enteral, as this route has been shown to have benefits over other regimens. However, PN is indicated in patients with severe AP who do not tolerate EN or who are unable to tolerate targeted requirements, or if there exists contraindication for EN overall. Complications of severe AP, which may occur and represent

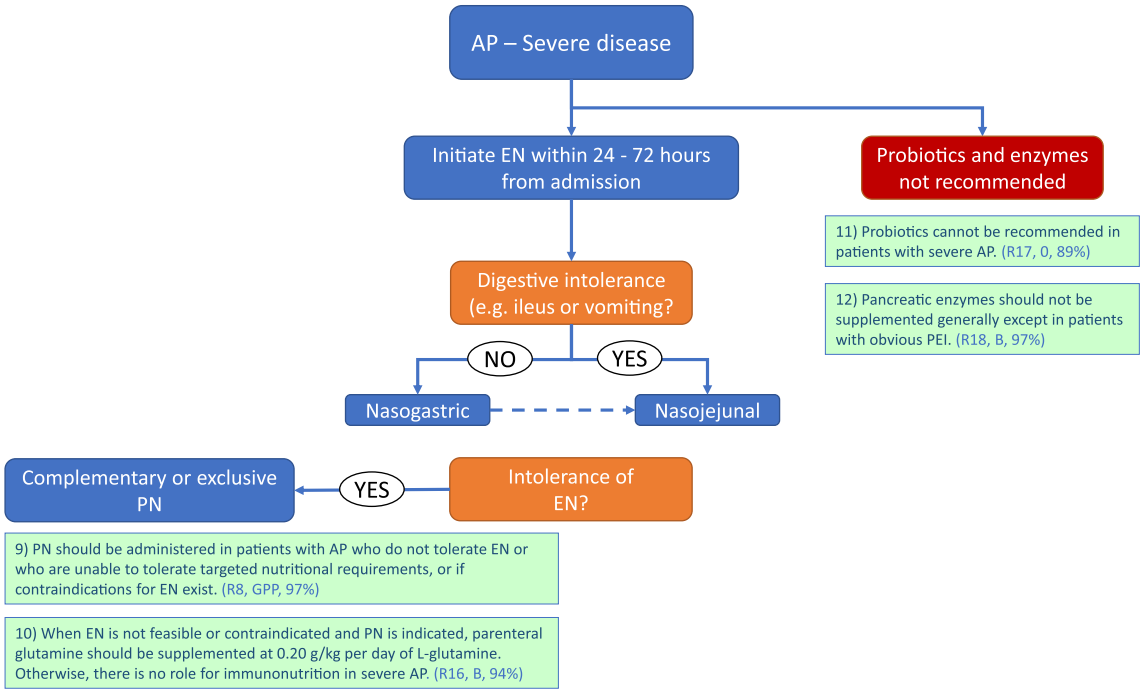

Fig. 3. Management of severe pancreatitis. AP, acute pancreatitis; EN, enteral nutrition; PEI, pancreatic exocrine insufficiency; PN, parenteral nutrition.

a contraindication for EN, include bowel obstruction, abdominal compartment syndrome, prolonged paralytic ileus and mesenteric ischemia [59]. Similar to critically ill patients with other diseases, approximately 20 % of patients with severe AP have complications, which are associated with absolute or relative contraindications for EN [16].

10) **When enteral nutrition is not feasible or contraindicated and parenteral nutrition is indicated, parenteral glutamine should be supplemented at 0.20 g/kg per day of L-glutamine. Otherwise, there is no role for immunonutrition in severe acute pancreatitis.**

(R16, grade B, strong consensus, 94 %)
Commentary

An initial meta-analysis including eleven RCTs assessed the effect of antioxidants (five RCTs on glutamine and six on various other antioxidants) on the outcome of patients with AP [60]. Among patients with AP, antioxidant therapy resulted in a borderline significant reduction in hospital stay, a significant decrease in complication rate and a non-significant decrease in mortality rate. Nevertheless, these results were mostly attributed to the effect of glutamine. Recently, a Cochrane Review assessed the effects of different pharmacological interventions including antioxidants in patients with AP [61]. Very low-quality evidence suggested that none of the pharmacological treatments decreased short-term mortality in patients with AP.

Regarding glutamine, four meta-analyses have been published. A meta-analysis of ten RCTs including 433 patients with severe AP revealed a significant decrease in the incidence of infectious complications and mortality in the patient group with glutamine-enriched nutrition [62]. Another meta-analysis of twelve RCTs (including 505 patients) demonstrated a significantly reduced infection rate and mortality after glutamine supplementation in patients with AP [63]. In the subgroup analyses, only patients who received total PN demonstrated a significant benefit in terms of study outcomes. Two recently published meta-analyses showed beneficial effects of glutamine supplementation in patients with AP in the terms of elevation of serum albumin concentrations, decrease in serum concentrations of C-reactive protein, and reductions in infectious complications, mortality and hospital stay [60,64]. Nevertheless, the risk of bias of the included studies is important due to many reasons: (i) small sample size (ii) possible heterogeneity and (iii) confounding factors.

3.2.2. *Substances not recommended in severe disease*

11) **Probiotics cannot be recommended in patients with severe acute pancreatitis.**

(R17, grade 0, consensus, 89 %)
Commentary

A meta-analysis of six RCTs including 536 patients revealed no significant benefit of probiotics on pancreatic infection rate, overall infection rate, operation rate, length of hospital stay and mortality [65]. Significant heterogeneity was observed in the type, dose and treatment duration of probiotics in these trials. In one of these RCTs the patient group assigned to a particular combination of probiotic strains showed similar pancreatic infection rate but increased mortality when compared with the placebo group [66].

12) **Pancreatic enzymes should not be supplemented generally except in patients with obvious pancreatic exocrine insufficiency.**

(R18, grade B, strong consensus, 97 %)
Commentary

There are only two RCTs with a total of 78 patients randomized to pancreatic enzyme supplementation or placebo [67,68]. In the study by Kahl et al. 20 of the 56 patients showed low fecal elastase values indicating pancreatic exocrine insufficiency (PEI). Although the pancreatic enzyme supplement group showed a tendency for better outcome this did not reach statistical significance [67]. In the second small study by Patankar et al. there was also no significant

difference in laboratory or clinical outcomes [68]. Therefore, no conclusion can be drawn, but enzyme supplementation should be considered in patients with proven or obvious PEI and malabsorption with steatorrhea.

3.3. Acute pancreatitis – severe disease with necrosectomy (Fig. 4)

3.3.1. Oral feeding with low fat soft diet

13) **Oral food intake in patients undergoing minimally invasive necrosectomy is safe and feasible and should be initiated in the first 24 h after the procedure, if the clinical state (hemodynamic stability, septic parameters, gastric emptying) of the patient allows it.**

(R9, grade GPP, strong consensus, 95 %)
Commentary

Patients with ANP have moderate or severe forms of AP, and a higher risk for development of multiple organ failure, secondary infection of the necrosis, and death [69]. After proven benefits of the "step-up" (minimally invasive approach) over the open approach for the treatment of ANP, minimally invasive techniques have been used extensively [70,71]. To date there are limited published data on nutritional support in patients with ANP treated by the minimally invasive approach (endoscopic, radiological, or minimal invasive surgery). In a comparative trial including patients undergoing endoscopic or surgical step-up approach for infected necrotizing pancreatitis [72], all patients received oral nutrition, if tolerated. If not, a nasojejunal feeding tube was introduced and EN was started. If gastrointestinal feeding was contraindicated, the patient received PN.

3.3.2. Enteral nutrition in case of intolerance to oral feeding or insufficiency of oral feeding

14) **In patients undergoing minimally invasive necrosectomy who are unable to be fed orally, EN is indicated via nasojejunal as preferred route.**

(R10, grade B, strong consensus, 91 %)
Commentary

See commentary to recommendation 10. In the RCT by Bakker et al. [43], showing no superiority of early (first 24 h) nasojejunal tube feeding when compared with an oral diet after 72 h, interventional procedures included percutaneous catheter drainage, endoscopic transgastric drainage or necrosectomy and surgical necrosectomy (invasive or open approach). The authors did not find any difference in the number of patients who underwent interventions between the groups. In a retrospective series of 37 patients undergoing laparoscopic transgastric necrosectomy, an oral food intake 24–48 h after the procedure was feasible and safe [64]. In one prospective study on video-assisted retroperitoneal debridement, 40 patients were fed by nasojejunal tube as the preferred route when tolerated; otherwise, PN was given [65]. Therefore, based on small series, nasojejunal feeding seems safe in patients having undergone minimally invasive necrosectomy.

3.3.3. Complementary or exclusive parenteral nutrition in case of intolerance to enteral nutrition

15) **Parenteral nutrition is indicated in patients undergoing minimally invasive necrosectomy who do not tolerate EN or who are unable to tolerate targeted nutritional requirements, or if there exist contraindications for enteral nutrition.**

(R11, grade GPP, strong consensus, 94 %)
Commentary

See commentary to recommendations 10 and 11.

3.3.4. Measurement of intra-abdominal pressure

16) **In patients with severe acute pancreatitis and intra-abdominal pressure 15 mmHg early enteral nutrition shall be initiated via nasojejunal, as the preferred route, or nasogastric tube. Intra-abdominal pressure and the clinical condition of patients during enteral nutrition shall be monitored continuously.**

(R12, grade A, strong consensus, 91 %)
Commentary

Although, it has been clearly demonstrated that EN in patients with severe AP reduces mortality and infectious complications, it has been reported to potentially increase intraluminal pressure with subsequent elevation of intra-abdominal pressure (IAP) and development of severe complications [73,74]. In an observational study, 274 patients with AP had intra-abdominal hypertension (IAH) and 103 developed an acute compartment syndrome (ACS). The intolerance of EN was more frequent in patients with grade III and IV IAH (n = 105) and 62/105 (59 %) required PN [75]. In only one RCT including 60 patients, comparing early with delayed EN in patients with IAH and severe AP, it was found that early EN had benefits in patients with IAP <15 mmHg preventing development of IAH [76].

17) **In patients with severe acute pancreatitis and intra-abdominal pressure > 15 mmHg enteral nutrition should be initiated via nasojejunal route starting at 20 mL/h, increasing the rate according to the tolerance. Temporary reduction or discontinuation of enteral nutrition should be considered when intra-abdominal pressure values further increase under enteral nutrition.**

(R13, grade B, strong consensus, 94 %)
Commentary

Because the majority of patients with IAH present digestive intolerance, EN should be initiated with caution via nasojejunal tube, starting at 20 ml/min and increasing the rate progressively, according to the IAP measurement [77].

18) **In patients with severe acute pancreatitis and intra-abdominal pressure > 20 mmHg or in the presence of acute compartment syndrome, enteral nutrition should be (temporarily) stopped and parenteral nutrition should be initiated.**

(R14, grade GPP, strong consensus, 94 %)
Commentary

In patients with IAP above 20 mmHg or in the presence of ACS, EN should be stopped and total PN should be initiated [74].

3.3.5. Open abdomen

19) **In patients with severe acute pancreatitis and open abdomen enteral nutrition should be administered, at least in a small amount. If required for achievement of nutritional requirements, supplementary or total parenteral nutrition should be added.**

(R15, grade B, strong consensus, 97 %)
Commentary

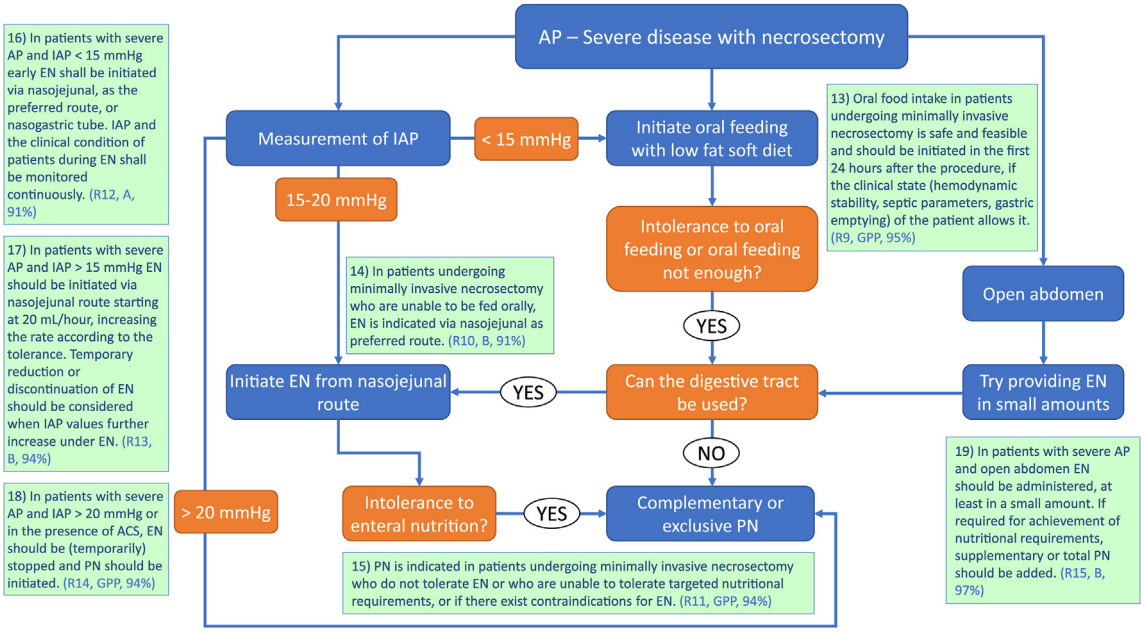

Fig. 4. Management of severe pancreatitis with necrosectomy. ACS, abdominal compartement syndrome; AP, acute pancreatitis; EN, enteral nutrition; IAP, intra-abdominal pressure; PN, parenteral nutrition.

A decompressive laparotomy (laparostomy) may be necessary in up to 74 % of patients who develop ACS during course of AP [78]. Several cohort studies reported that initiation and feeding by EN was feasible and safe despite a relatively high rate of digestive intolerance, ranging from 48 to 67 % [79–84]. Two studies concluded that early EN in patients with an open abdomen resulted in higher fascial closure rates, lower fistula rates, reduced nosocomial infections and lower hospital costs [83,84].

4. Chronic pancreatitis (Fig. 5)

20) **Risk of malnutrition in chronic pancreatitis is high and malnutrition is common in patients with chronic pancreatitis.**

(S2, strong consensus, 100 %)
Commentary

Malnutrition is often a late, but important manifestation in the course of CP and depends on the intensity and duration of the underlying disease. The latency between onset of first symptoms and signs of CP, including pain and malabsorption/malnutrition is between five to ten years in alcoholic, but delayed in non-alcoholic pancreatitis [4,85].

Despite the inconsistency of the data there is an evident risk of malnutrition in patients with CP [86–88]. According to a recent study medium or higher risk for malnutrition based on Malnutrition Universal Screening Tool (MUST) score of one or higher was found in 31.5 % patients [89]. Similarly, 26 % underweight patients with a nutritional risk were identified in a study of outpatients with CP [90].

In patients with CP with moderate to severe weight loss, decreased lean body mass and sarcopenia may lead to decreased functional capacity, which may have an impact on quality of life [91–93]. In addition, PEI leads to the increased risk of developing significant bone loss and severe osteoporosis [94,95]. A recent prospective study [93] including 182 patients with CP showed that sarcopenia was present in 17 % (74 % of patients with CP had a BMI >18.5 kg/m^2). During follow-up, sarcopenia was associated with an increased risk of hospitalization (OR 2.2; 95 % CI 0.9 to 5.0; $p = 0.07$), increased number of in-hospital days ($p < 0.001$), and reduced survival (HR 6.7; 95 % CI 1.8 to 25.0; $p = 0.005$).

21) **Pancreatic insufficiency, abdominal pain, alcohol abuse, lower food intake, diabetes mellitus and smoking are the main causes of malnutrition in chronic pancreatitis.**

(S3, strong consensus, 97 %)
Commentary

Multiple risk factors for developing nutrient deficiencies and malnutrition co-exist in patients with CP. First of all, pancreatic insufficiency (exocrine but also often endocrine) can lead to maldigestion and malabsorption. Clinical signs of PEI include steatorrhea, abdominal pain, weight loss and malnutrition [4]. Recent data showed endocrine insufficiency and/or clinical steatorrhea in 41 % and 36 % of 809 patients [96]. Moreover, increased resting energy expenditure can be seen in up to 50 % of patients with CP, thus leading to a negative energy balance and malnutrition [97]. Furthermore, abdominal pain, which is frequent in patients with CP, can lead to suboptimal dietary intake and also contribute to malnutrition [4].

Tobacco is an independent risk factor for CP, and can also be a disease modifier, acting in synergy with alcohol intake, and therefore, adds to the nutritional risk factors [96].

4.1. Diagnostics

4.1.1. Evaluation of nutritional status and screening for micro- and macronutrient deficiencies (Fig. 6)

22) **Nutritional status should be assessed according to symptoms, organic functions, anthropometry, and biochemical values. Solely body mass index should not be used, because it does not register sarcopenia in the obese patient with chronic pancreatitis.**

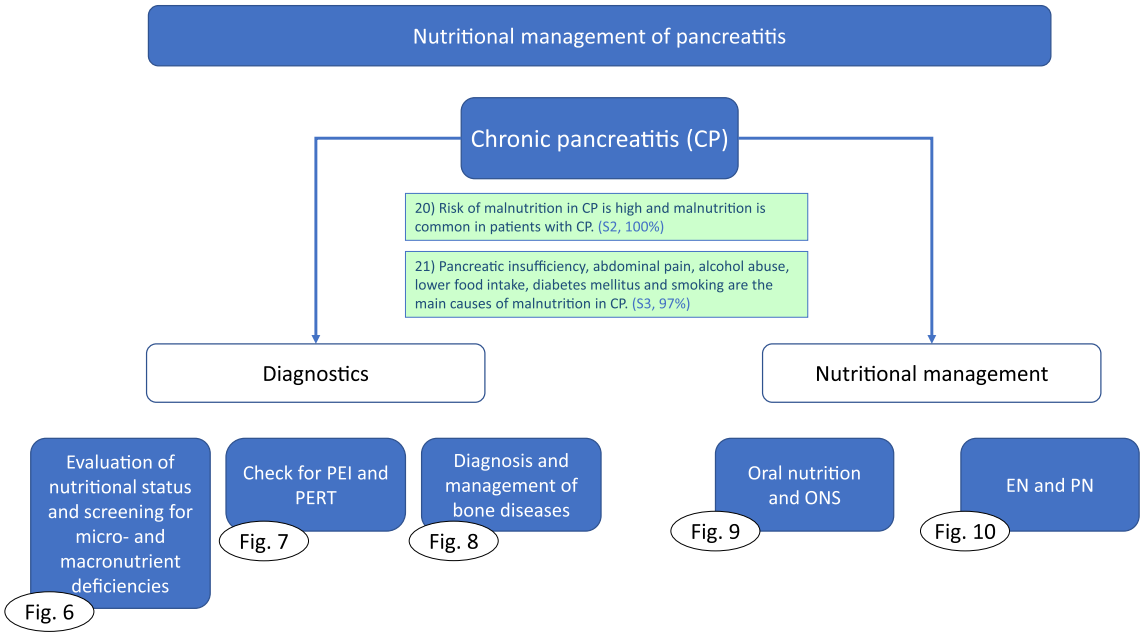

Fig. 5. Nutritional management of chronic pancreatitis. CP, chronic pancreatitis; EN, enteral nutrition; ONS, oral nutritional supplements; PEI, pancreatic exocrine insufficiency; PERT, pancreatic enzyme replacement therapy; PN, parenteral nutrition.

(R19, grade GPP, strong consensus, 97 %)

Commentary

Studies assessing malnutrition have identified many biochemical factors that are associated with malnutrition [98,99] and prevalence studies show a diverse presentation of malnutrition. Olesen et al. identified that 26 % of patients with CP were underweight in a cross-sectional study of 166 patients with CP [90], whereas Duggan et al. highlighted that over half of the patients in their prospective controlled cohort study (n = 128) fell into the overweight/obese category using BMI [91]. However, patients had lower muscle stores and reduced functional status assessed using hand-grip strength than healthy controls. Consequently, BMI alone is not considered an adequate method of assessing nutritional status. Percentage weight loss is considered a more reliable indicator of the onset of malnutrition and is associated with an increased risk in the surgical setting [100].

Consequently, nutritional assessment should allow for detection of simple malnutrition, sarcopenia and micronutrient deficiencies in addition to identifying symptoms that may predispose patients to worsening malnutrition.

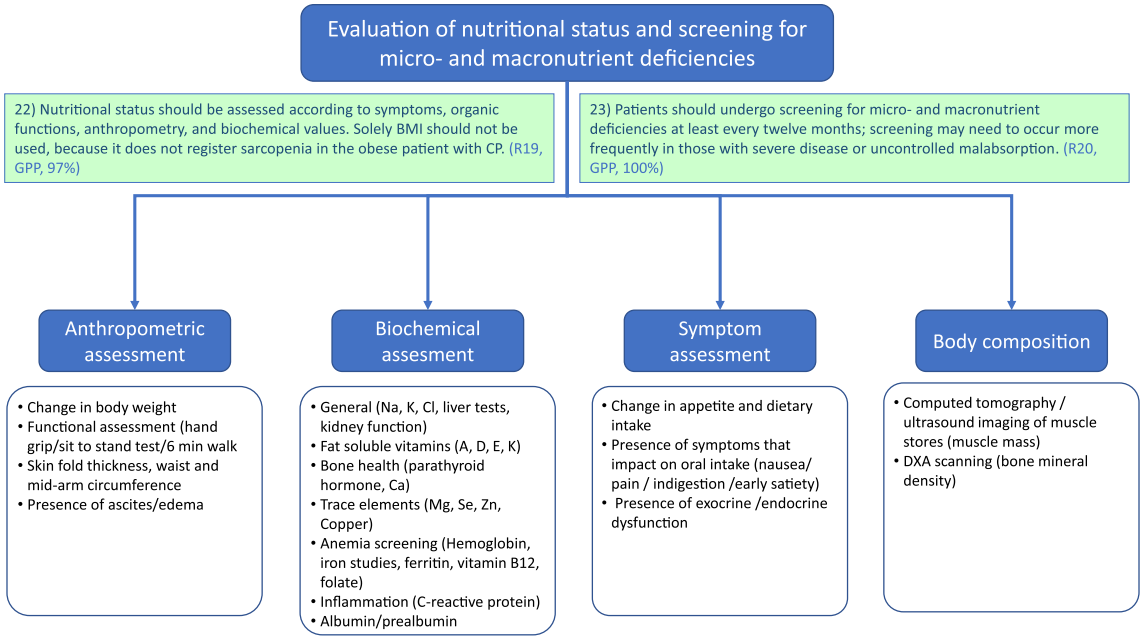

Fig. 6. Evaluation of nutritional status and screening for micro- and macronutrient deficiencies in chronic pancreatitis. CP, chronic pancreatitis; DXA, dual energy X-ray absorptiometry.

23) **Patients should undergo screening for micro- and macronutrient deficiencies at least every twelve months; screening may need to occur more frequently in those with severe disease or uncontrolled malabsorption.**

(R20, grade GPP, strong consensus, 100 %)
Commentary

Patients with CP are at high risk of malnutrition, both in terms of body weight and altered body composition [91]. This has an impact on quality of life [90] and survival after surgery [101,102]. Nutritional intervention can improve nutritional markers and is associated with reduced pain [103] and, therefore, routine screening to trigger nutritional intervention should be undertaken. Deficiencies in micronutrients (vitamin B12, folic acid, vitamin A, D and E, zinc, selenium, iron) are well documented in patients with PEI, these are diverse in presentation with some studies reporting biochemical deficiencies [91,94,104] and case reports document clinical manifestations including night blindness [105,106]. However, there are no data recommending the frequency of assessment or the likely timing of progression to micronutrient deficiency. As clinical manifestation of deficiency represents a late presentation, routine screening should be implemented to detect early signs of deficiency.

4.1.2. Check for exocrine insufficency and pancreatic enzyme replacement therapy (Fig. 7)

24) **When pancreatic exocrine insufficiency is diagnosed through clinical signs and symptoms and/or laboratory tests of malabsorption, pancreatic enzyme replacement therapy shall be initiated. An accurate nutritional assessment is mandatory to detect signs of malabsorption.**

(R34, grade A, strong consensus, 100 %)
Commentary

The most frequent clinical sign of PEI is steatorrhea [107], defined as presence of fat in the stool, and associated generally with flatulence, bloating, dyspepsia, urgency to pass stools, and cramping abdominal pain. In a recent systematic review, including 14 studies on pancreatic enzyme supplementation in patients with CP, the criteria for the diagnosis of PEI were the measurement of the coefficient of fat absorption with a threshold <80 % or the fecal fat absorption less than 7–15 g of fat per day [108].

PEI is consistently associated with biochemical and clinical signs of malnutrition Management of PEI involves replacing the inadequate pancreatic enzymes, which should be used to maintain weight and improve the symptoms of maldigestion [109,110].

Awareness of PEI among many physicians is poor outside of referral centers and especially among physicians in primary care [111,112]. Nevertheless, untreated PEI has also a deleterious impact on the quality of life of patients [113]. It is recommended that enzyme replacement is started when clinical signs of malabsorption, or anthropometric and/or biochemical signs of malnutrition are present [87,114–117]. Symptoms include weight loss, alteration of body compartments at bioimpedance analysis, and low nutritional markers (albumin, cholinesterase, prealbumin, retinol-binding protein, and magnesium) [114,118–121].

25) **pH-sensitive, enteric-coated microspheres pancreatic enzyme replacement preparations shall be used for treating pancreatic exocrine insufficiency.**

(R35, grade A, strong consensus, 100 %)
Commentary

Several factors affect the efficacy of pancreatic enzyme supplementation: (i) mixture with meal; (ii) gastric emptying with meal; (iii) mixing with chyme and bile acids and rapid release of enzymes in duodenum [122].

Nowadays, most of the pancreatic enzyme preparations are formulated as pH-sensitive, enteric-coated, capsules containing microspheres or tablets that protect the enzymes from gastric acidity and allow them to disintegrate rapidly at pH > 5.5 in the duodenum [122–124].

The efficacy of these more recent formulations has been demonstrated in several recent studies [125–128] and in a recent meta-analysis [108]. A Cochrane review on the efficacy of pancreatic enzyme preparations in patients with pancreatic insufficiency demonstrated a higher efficacy for enteric-coated microspheres

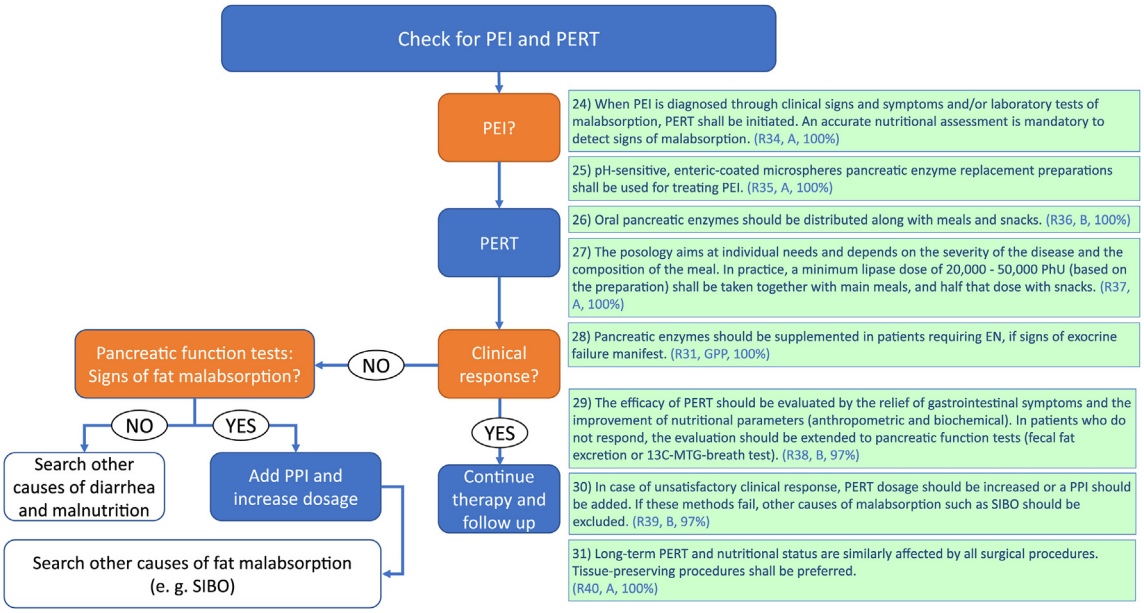

Fig. 7. Check for pancreatic exocrine insufficiency and pancreatic enzyme replacement therapy in chronic pancreatitis. EN, enteral nutrition; PEI, pancreatic exocrine insufficiency; PERT, pancreatic enzyme replacement therapy; PPI, proton pump inhibitor; SIBO, small intestinal bacterial overgrowth.

compared with enteric-coated tablets [129]. Mini-microspheres 1.0–1.2 mm in diameter seem to be associated with higher therapeutic efficacy compared with 1.8–2.0 mm microspheres that still have an optimal therapeutic action [130]. Another trial compared two enteric-coated pancreatic enzyme preparations. One moisture-resistant, formulated to contain between 90 % and 110 % labeled lipase content over the shelf life of the product and the other potentially unstable in the presence of moisture and degradable over time. The characteristics of the moisture-resistant formulation should have allowed more accurate dosing, both providing more predictable therapeutic effects and reducing the risk of overdose, which is assumed as a potential risk factor for fibrosing colonopathy. The results suggested a comparable efficacy and safety in patients with cystic fibrosis for the treatment of PEI [131].

26) **Oral pancreatic enzymes should be distributed along with meals and snacks.**

(R36, grade B, strong consensus, 100 %)
Commentary

The efficacy of pancreatic enzyme supplements presupposes the mixing of enzymes and chyme [123]. While one study evaluating the impact of the scheduling of pancreatic enzyme replacement therapy (PERT) administration on fat malabsorption suggested the optimal timing of administration was during or after meals, no significant difference was observed when patients took PERT immediately before meals [132]. In practice, although many patients prefer to take PERT at the beginning of meals, they should be encouraged to spread the capsules out over a meal when using multiple capsules or with larger meals [124,132]. If the patient is taking the older preparations of pancreas powder, they should take about a third of the dose immediately before, one third during, and one third immediately after the meal. This concerns only meals and snacks that contain fat (e.g. not for fruit).

27) **The posology aims at individual needs and depends on the severity of the disease and the composition of the meal. In practice, a minimum lipase dose of 20,000–50,000 PhU (based on the preparation) shall be taken together with main meals, and half that dose with snacks.**

(R37, grade A, strong consensus, 100 %)
Commentary

The dosage recommended depends on the patient's clinical response, but the dosage and dosing will need to be monitored carefully, as well as altered, depending on patient's food intake/pattern of eating, method of cooking, portion sizes, and disease evolution.

For the digestion of a normal meal a minimum activity of 30,000 IU of naturally secreted pancreatic lipase is required. The recommended initial dose is about 10 % of the physiologically secreted dose of lipase after a normal meal [133]. Since 1 IU of naturally secreted lipase equals 3 PhU in commercial preparations, the minimum amount of lipase needed for digestion of a normal meal is 90,000 PhU (endogenous plus orally administered lipase).

The results of several RCTs have proven the efficacy of PERT with enteric-coated mini-microspheres at a dose ranging from 40,000–80,000 PhU of lipase per main meal, and half dose per snack [127,128,132,134–136]. Studies evaluating enteric-coated microspheres have shown a similar efficacy for doses ranging from 10,000–40,000 PhU of lipase per meal, indicating the lack of a dose-response relationship with these preparations [137,138].

Dose escalation may be warranted according to response. In adults there is no upper limit to dosing, as there is no risk of overdose because pancreatic enzymes exceeding the needs are eliminated through stools. Caution for dosage should be placed in children in whom colonic strictures have been described after high dose of the enteric coated, delayed release preparations [139].

28) **Pancreatic enzymes should be supplemented in patients requiring enteral nutrition, if signs of exocrine failure manifest.**

(R31, grade GPP, strong consensus, 100 %)
Commentary

In patients with exocrine failure, who do not improve with semi-elemental formulae, pancreatic enzymes can be administered with the formula [140]. This involves opening the capsules and suspending the enzyme microspheres in thickened acidic fluid (such as the mildly thickened or “nectar-thick” fruit juice used for dysphagia) for delivery via the feeding tube.

29) **The efficacy of pancreatic enzyme replacement therapy should be evaluated by the relief of gastrointestinal symptoms and the improvement of nutritional parameters (anthropometric and biochemical). In patients who do not respond, the evaluation should be extended to pancreatic function tests (fecal fat excretion or ^{13}C-MTG-breath test).**

(R38, grade B, strong consensus, 97 %)
Commentary

The aforementioned recent meta-analysis including 14 RCTs [108] showed that PERT increased the coefficient of fat absorption, as well as improved gastrointestinal symptoms, compared with baseline or placebo. Two open label extensions up to one year from RCTs included in the meta-analysis demonstrated significant improvement in nutritional parameters and weight [126,141]. A review of reported data [98] as well as the recent guidelines on the therapy for CP [4] support the use of nutritional parameters as an optimal way to assess the efficacy of PERT. Dietary intake and nutritional status should be monitored regularly to maximize patient compliance and specialist dietetic assessment sought in patients with underlying malnutrition [142].

In patients who do not respond, pancreatic function tests [108] while on PERT can monitor effectiveness. ^{13}C-MTG-breath test is a useful method that can replace the somewhat cumbersome fecal fat excretion tests and can be used for patients on PERT [143].

30) **In case of unsatisfactory clinical response, pancreatic enzyme replacement therapy dosage should be increased or a protein pump inhibitor should be added. If these methods fail, other causes of malabsorption such as small intestinal bacterial overgrowth should be excluded.**

(R39, grade B, strong consensus, 97 %)
Commentary

The recommended dose of 20,000–50,000 PhU with main meals has been shown to improve symptoms in more than half the patients [108]. Dose escalation may be warranted according to response. In adults there is no upper limit to dosing, as there is no risk of overdose because pancreatic enzymes exceeding the needs are eliminated in the stool. Caution for high PERT dosage should be exercised in children, in whom colonic strictures have been described after high dose of the enteric coated, delayed release preparations [139].

The inhibition of gastric acid secretion by proton pump inhibitors (PPI) can lead to a significant improvement and even

normalization of fat digestion in patients with an incomplete response to PERT, as shown in a prospective cohort study of 21 patients with CP (43 % had an initial incomplete response to PERT, and 29 % normalized their function after addition of a PPI) [144]. Nevertheless, a review including 34 clinical trials failed to show improvement in the efficacy of PERT with PPI or histamine-2 receptor antagonists [145]. It is noteworthy that the populations included and the therapeutic schemes were very heterogeneous, therefore, suggesting significant bias.

Small intestinal bacterial overgrowth (SIBO) can also explain persistent symptoms. A recent prospective case–control study revealed that SIBO was present in 15 % of patients with CP whereas no healthy control was tested positive by means of a fasting glucose hydrogen breath test [146].

31) **Long-term pancreatic enzyme replacement therapy and nutritional status are similarly affected by all surgical procedures. Tissue-preserving procedures shall be preferred.**

(R40, grade A, strong consensus, 100 %)
Commentary

Common indications for surgical intervention in CP include poorly controlled pain, duodenal, biliary and pancreatic duct obstruction, and suspicion of cancer [147].

Surgery for CP can be broadly classified into three categories: drainage procedures, partial pancreatic resection including or not the duodenum, and total pancreatectomy.

Theoretically, the type of procedure may deeply affect short- and long-term nutritional outcomes, since the extension of the parenchyma resection, as well as the preservation of the duodenum and bile natural transit, and pancreatic secretion may represent key factors for endocrine and exocrine functions [148,149].

Meta-analyses showed better postoperative pain relief and improved quality of life with the Beger procedure compared with conventional pancreaticoduodenectomy [150,151]. However, the studies included had a high grade of heterogeneity and a recent large prospective large RCT showed no significant difference between procedures in the long-term nutritional status, quality of life, and preservation of the exocrine pancreatic function [152].

A 2015 meta-analysis of 23 studies compared outcomes of the Frey procedure with pancreaticoduodenectomy and the Berger procedure [153]. Short-term quality of life and pancreatic function outcomes were more favorable in patients who had the Frey procedure than in those who had pancreaticoduodenectomy. Long-term follow-up data from an RCT comparing the Frey and Berger procedures for CP showed no significant difference in endocrine or exocrine insufficiency more than a decade after surgery [154].

4.1.3. Diagnosis and management of bone diseases (Fig. 8)

32) **Patients with chronic pancreatitis are at risk for osteoporosis (almost one out of four) and at high risk (about two out of three), for osteopathy (either osteoporosis or osteopenia).**

(S6, strong consensus, 97 %)
Commentary

A systematic review and meta-analysis including ten studies revealed, of the total 513 patients with CP included, a pooled prevalence rate of osteoporosis of 24.3 % (95 % CI 16.6–32.0 %) and osteopathy (either osteoporosis or osteopenia) of 65 % (95 % CI 54.7–74.0 %) [155]. Two of the included studies revealed osteoporosis rate for controls respectively 8.6 and 10.2 %. Data suggest that vitamin D deficiency is not the sole driver of bone demineralization, other factors that may be of importance for premature bone demineralization in CP are heavy smoking, low physical activity, and chronic inflammation [156].

The important clinical endpoint of osteoporosis is bone fracture. Two large retrospective studies shed light on this regarding patients with CP. The first is a cohort database study, examining patients with CP at a single tertiary care center. A total of 3192 patients with CP and 1,436,699 controls were included in the study. The fracture prevalence (patients with fracture per total patients) was 1.1 % in controls (16,208/1,436,699) and 4.8 % in patients with CP (154/3192); in comparison Crohn's disease revealed a risk of 3.0 % (182/6057); liver cirrhosis 4.8 % (805/16,658) and celiac disease 5.0 % (74/1480) [157].

The second, a Danish retrospective cohort study including 2594 patients with CP revealed an adjusted hazard ratio for any fracture of 1.7 (95 % CI 1.6 to 1.8) [158]. Patients with CP receiving PERT for fat malabsorption had a lower risk of fractures than other CP patients (HR 0.8; 95 % CI 0.7 to 0.9).

33) **Basic preventive measures should be advised to all patients with chronic pancreatitis including adequate calcium/vitamin D intake and, if indicated, pancreatic enzyme supplementation, regular weight-bearing exercise and smoking and alcohol avoidance. Additional pharmacologic treatment should be reserved for patients with osteopathy and, in particular, osteoporosis.**

(R42, grade GPP, strong consensus, 97 %)
Commentary

The reasons for osteopathy in CP are multifactorial; (i) low serum vitamin D concentrations due to impaired absorption of fat-soluble vitamin D, poor dietary intake (including calcium) and/or sunshine exposure, (ii) smoking and alcohol intake, (iii) low physical activity, and (iv) chronic inflammation, all contribute. Therefore, basic preventive measures should be advised to all patients with CP including adequate calcium/vitamin D intake and PERT if indicated, regular weight-bearing exercise and avoidance of smoking and alcohol [4]. Research on pharmaceutical supplementation of vitamin D and calcium in patients with osteopenia and adding bisphosphonates in osteoporosis has mainly been performed in post-menopausal women and elderly patients. Based on these findings, and bearing in mind that the cost and side effects are limited, one could consider in patients with osteopathy to supplement vitamin D (800 IU) and calcium (500–1000 mg) daily [110]. In patients with osteopenia it is recommended to repeat the dual-energy X-ray absorptiometry (DXA) every two years, whereby in patients with osteoporosis there are no specific recommendations beside appropriate medication, screening for other causes and/or referral to a bone specialist [4].

34) **Dual-energy X-ray absorptiometry shall be used to identify patients with chronic pancreatitis with osteopathy.**

(R41, grade A, strong consensus, 100 %)
Commentary

The American College of Radiology aims to rate the appropriateness of several radiological modalities for specific patient populations. Although they do not mention CP explicitly, they do state that in premenopausal females and males 20–50 years of age with malabsorption, DXA of the lumbar spine and hip(s) or distal forearm is usually an appropriate diagnostic modality to identify low bone mineral density [159]. It is not yet well defined when and to

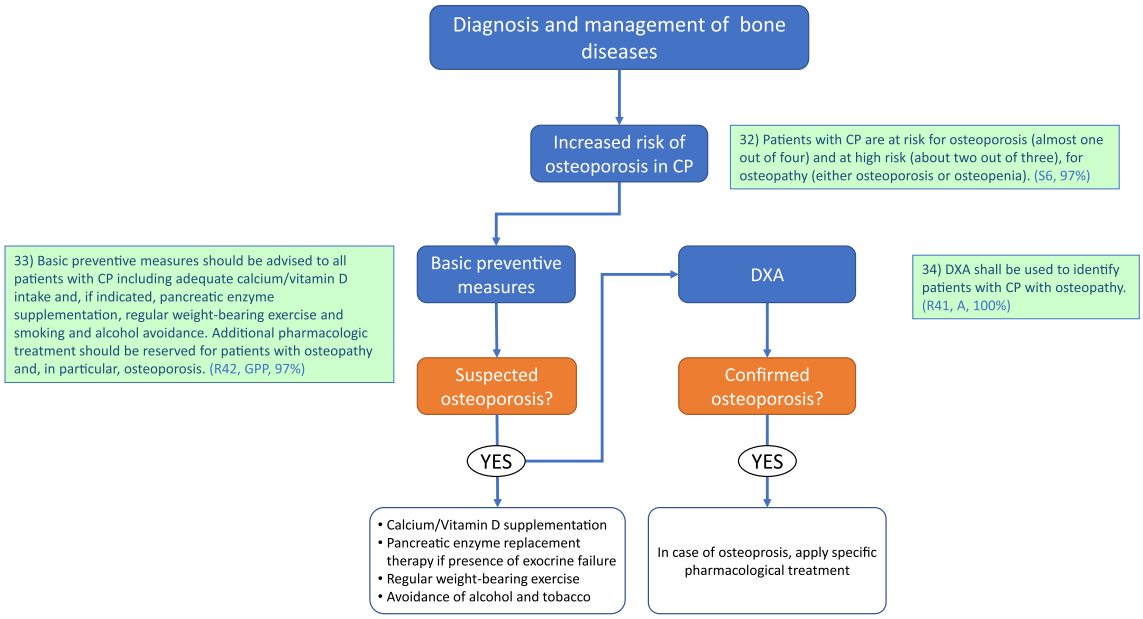

Fig. 8. Diagnosis and management of bone diseases. CP, chronic pancreatitis; DXA, dual energy X-ray absorptiometry.

whom these tests should be offered in patients with CP. However, there are recommendations from the American Gastroenterological Association on the detection of osteoporosis in other gastrointestinal diseases: recommending that patients with at least one additional osteoporosis risk factor should undergo initial screening with DXA [160]. This recommendation was specifically for inflammatory bowel disease, celiac disease, and post-gastrectomy patients. The recently published HaPanEU guidelines on CP argued that bone density testing by DXA should be extended to patients with CP with an additional risk; post-menopausal women, those with previous low-trauma fractures, men over 50 years and those with malabsorption [4]. They further stated that considering the associated morbidity and cost of bone fractures when prevention is within range [161], a baseline bone density assessment for all patients with CP may be worth considering.

4.2. Nutritional management

4.2.1. Oral nutrition (Fig. 9)

4.2.1.1. Well-nourished patients without deficiencies

35) **Patients with chronic pancreatitis do not need to follow a restrictive diet.**

(S4, strong consensus, 94 %).

36) **Chronic pancreatitis patients with a normal nutritional status should adhere to a well-balanced diet.**

(R21, grade GPP, strong consensus, 94 %)
Commentary

There are very little data to suggest the optimal dietary management for patients with CP. Historically, patients were encouraged to have a low-fat diet, and studies in the Netherlands suggest 48–58 % of patients still restrict dietary fat [95,111]. International guidelines are consistent in their recommendation that patients should have a balanced diet and avoid fat restriction [4,162–165]. The role of dietary fat has been examined in small studies, suggesting an improvement in dyspeptic symptoms in patients with very mild pancreatic disease who did not consume alcohol regularly when a very low fat diet was consumed (<20 g fat per day) [166] and patients who consumed a higher fat diet were thought to be diagnosed at a younger age, and had an increased probability of continuous abdominal pain [167] suggesting a potential role in the initial development of CP. However once CP was diagnosed, there was no difference in severity or complications of disease. An RCT comparing dietary counselling and nutritional supplements in a cohort of 60 malnourished patients with CP found that nutritional intervention in which 33 % of energy was derived from fat was well tolerated [103]. Improvements in nutritional status and pain control were observed in patients receiving nutritional intervention and the authors did not report any adverse events [103].

37) **In patients with chronic pancreatitis, diets very high in fiber should be avoided.**

(R23, grade B, strong consensus, 91 %)
Commentary

Patients consuming very high fiber diets reported increased flatulence, and increased fecal weight and fat losses were observed in a small trial (n = 12) in patients with CP [168].

38) **In patients with chronic pancreatitis, there is no need for dietary fat restriction unless symptoms of steatorrhea cannot be controlled.**

(S5, strong consensus, 100 %)

4.2.1.2. Malnourished patients

39) **Malnourished patients with chronic pancreatitis should be advised to consume high protein, high-energy food in five to six small meals per day.**

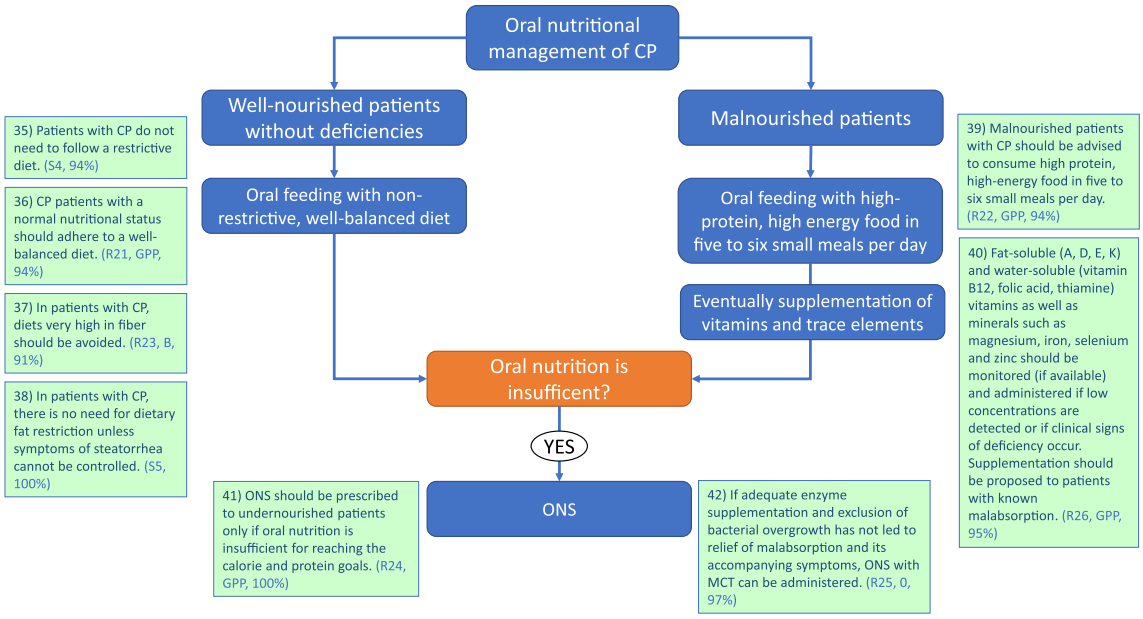

Fig. 9. Oral nutritional management of chronic pancreatitis. CP, chronic pancreatitis; MCT, medium chain triglycerides; ONS, oral nutritional supplements.

(R22, grade GPP, strong consensus, 94 %)
Commentary
See commentary to recommendation 36.

40) **Fat-soluble (A, D, E, K) and water-soluble (vitamin B12, folic acid, thiamine) vitamins as well as minerals such as magnesium, iron, selenium and zinc should be monitored (if available) and administered if low concentrations are detected or if clinical signs of deficiency occur. Supplementation should be proposed to patients with known malabsorption.**

(R26, grade GPP, strong consensus, 95 %)
Commentary
The reported prevalence of deficiency of fat-soluble vitamins is 3–14.5 % for vitamin A deficiency [91,94,169], 58–77.9 % for vitamin D deficiency [91,94,169,170], 9–24 % for vitamin E deficiency [91,94,98,169,170] and 13–63 % for vitamin K deficiency [91,94,169,170]. In a prospective controlled cohort study of 128 subjects and 66 age/gender-matched controls, 14.5 % and 24.2 % were deficient in vitamins A and E, respectively, with a significant difference compared with controls. Nineteen percent of patients had excess serum vitamin A concentrations [91]. This must be taken in account and a blind supplementation of all fat-soluble vitamins for all patients with CPs is not advised.

Deficiencies of water-soluble vitamins in patients with CP are less frequent. A recent study with 301 patients with CP and 266 controls showed that patients with CP had significantly lower concentrations of vitamins A, D and E, but no difference regarding vitamin B12 [94]. Similarly, another cohort study of 114 patients with CP (33 % with exocrine failure) did not show any significant deficiencies of vitamin B12 (0 %) and folic acid (2.2 %) [114].

Thiamine deficiency secondary to concomitant alcoholism must be considered [98].

Minerals and trace elements deficiencies have been reported in patients with CP in some case–control studies. The results are conflicting. Lower concentrations of zinc, selenium [98] and magnesium [114] have been observed. Furthermore, low magnesium concentrations seemed to correlate with exocrine failure [114].

4.2.2. *Oral nutritional supplements (Fig. 9)*

41) **Oral nutritional supplements should be prescribed to undernourished patients only if oral nutrition is insufficient for reaching the calorie and protein goals.**

(R24, grade GPP, strong consensus, 100 %)
Commentary
Very few studies have investigated the benefit of oral nutritional supplements (ONS) in patients with CP. Eighty percent of patients can be treated with diet and enzyme supplementation, the rest need oral supplementation [87]. ONS can be of benefit in undernourished patients with CP, especially if the caloric and protein goals cannot be reached with normal meals and counselling. ONS are a simple way to improve oral intake, but long-term compliance may be a problem.

42) **If adequate enzyme supplementation and exclusion of bacterial overgrowth has not led to relief of malabsorption and its accompanying symptoms, oral nutritional supplements with medium chain triglycerides can be administered.**

(R25, grade 0, strong consensus, 97 %)
Commentary
There are no RCTs investigating the relative efficacy of different formulae (e.g. standard or peptide-based with medium chain triglycerides (MCT)). However, in the presence of PEI, enteral formulae consisting of pre-digested products and a mixture of long chain fatty acids and MCT would seem, theoretically, to have potential advantage. MCTs are less dependent on lipase activity for their absorption [171]. A reduction in oral fat intake or the replacement of dietary fat with MCT risks a reduction in energy intake and, therefore, a negative energy balance. MCTs have an unpleasant taste and are associated with adverse effects like cramps, nausea, and diarrhea. Up to now, studies have not shown any clear benefit of MCTs over standard long-chain triglycerides when used in combination with enzyme supplementation [171,172]. One RCT investigated the efficacy of ONS in patients with

CP and severe malnutrition [103]. Dietary counselling achieved equal results compared with the use of a commercial supplement enriched with MCTs. Both groups also received enzyme supplementation and so it is not possible to explain the additional gain from dietary MCTs over enzyme supplementation.

4.2.3. Enteral nutrition (Fig. 10)

43) **Enteral nutrition should be administered in patients with malnutrition who are not responding to oral nutritional support.**

(R27, grade GPP, strong consensus, 100 %)
Commentary

Oral nutritional support with dietary counselling is usually sufficient to improve nutritional status in patients with CP [105]. EN is indicated in approximately 5 % of patients with CP [90]. Regarding indications and outcomes of EN in these patients, evidence is based on few cohort studies and RCTs are generally lacking [4].

44) **Enteral nutrition should be administered via the nasojejunal route in patients with pain, delayed gastric emptying, persistent nausea or vomiting and gastric outlet syndrome.**

(R28, grade GPP, strong consensus, 100 %)
Commentary

Four retrospective series have shown the benefits of EN in patients with CP regarding weight gain and pain control [173–176]. Two of them included 58 [174] and 50 patients [176] respectively, in whom a naso-jejunal tube was placed.

45) **Semi-elemental formulae with medium chain triglycerides can be used if standard formulae are not tolerated.**

(R30, grade GPP, strong consensus, 94 %)
Commentary

There is limited high quality evidence for the composition of enteral formulae in patients with CP. However, there is a rationale that semi-elemental enteral formulae with MCTs are more adapted for jejunal nutrition, compared with polymeric formulae [177]. In two of the aforementioned studies [174,176], semi-elemental formulae were used with good digestive tolerance. Nevertheless, the cost of these feeds is higher and data on cost-effectiveness are also lacking.

46) **Long-term jejunostomy access (percutaneous endoscopic gastrostomy with jejunal extension or direct percutaneous endoscopic jejunostomy or surgical jejunostomy) can be used in those requiring EN for more than 30 days.**

(R29, grade GPP, strong consensus, 97 %)
Commentary

Long-term access with a percutaneous endoscopic gastrostomy with jejunal extension or a direct percutaneous endoscopic jejunostomy was used in 57 [173] and 58 patients [175]. All studies showed that this type of nutritional support was safe and effective in patients with CP, even in case of gastric outlet syndrome [175,176].

4.2.4. Parenteral nutrition (Fig. 10)

47) **Parenteral nutrition may be indicated in patients with gastric outlet obstruction and in those with complex fistulating disease, or in case of intolerance of enteral nutrition.**

(R32, grade GPP, strong consensus, 100 %)
Commentary

PN is infrequently uses in patients with CP [4,88]. EN preserves immune function and mucosal architecture and decreases the

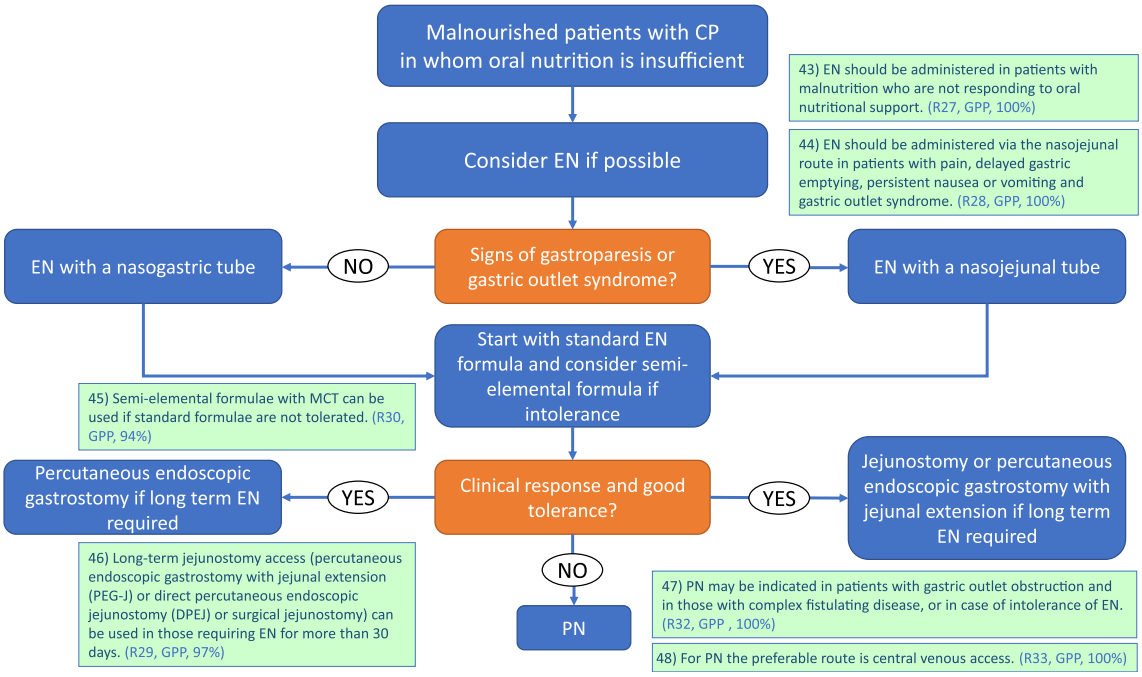

Fig. 10. Management of malnourished patients with chronic pancreatitis in whom oral nutrition is insufficient. CP, chronic pancreatitis; EN, enteral nutrition; MCT, medium chain triglycerides; PN, parenteral nutrition.

possibility for hyperglycemia while PN also increases the risk of catheter-related infections and septic complications [87,165]. PN is, therefore, only indicated when it is impossible to use EN (e.g. presence of gastric outlet obstruction, the need for gastric decompression, when it is impossible to introduce a tube into the jejunum, or a complicated fistula is present) or if requirements are only partly reached by EN.

48) **For parenteral nutrition the preferable route is central venous access.**

(R33, grade GPP, strong consensus, 100 %)
Commentary

PN is mainly administered over a short-term period and long-term studies are lacking. In this case, a standard nutritional solution should be administered via central venous access such as a peripherally inserted central catheter. Contraindications to PN do not differ from general contraindications to medical nutrition.

Funding statement

This guideline was solely financed by ESPEN, the European Society for Clinical Nutrition and Metabolism.

Conflict of Interest

The expert members of the working group were accredited by the ESPEN Guidelines Group, the ESPEN Education and Clinical Practice Committee, and the ESPEN executive. All expert members have declared their individual conflicts of interest according to the rules of the International Committee of Medical Journal Editors (ICMJE). If potential conflicts were indicated, they were reviewed by the ESPEN guideline officers and, in cases of doubts, by the ESPEN executive. None of the expert panel had to be excluded from the working group or from co-authorship because of serious conflicts. The conflict of interest forms are stored at the ESPEN guideline office and can be reviewed with legitimate interest upon request to the ESPEN executive.

References

[1] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–11.
[2] Arvanitakis M, Dumonceau JM, Albert J, Badaoui A, Bali MA, Barthet M, et al. Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. Endoscopy 2018;50:524–46.
[3] Trikudanathan G, Wolbrink DRJ, van Santvoort HC, Mallery S, Freeman M, Besselink MG. Current Concepts in severe acute and necrotizing pancreatitis: an evidence-based approach. Gastroenterology 2019;156:1994–2007 e3.
[4] Olesen SS, Poulsen JL, Drewes AM, Frokjaer JB, Laukkarinen J, Parhiala M, et al. The Scandinavian baltic pancreatic club (SBPC) database: design, rationale and characterisation of the study cohort. Scand J Gastroenterol 2017;52:909–15.
[5] Dumonceau JM, Delhaye M, Tringali A, Arvanitakis M, Sanchez-Yague A, Vaysse T, et al. Endoscopic treatment of chronic pancreatitis: European society of gastrointestinal endoscopy (ESGE) guideline - updated August 2018. Endoscopy 2019;51:179–93.
[6] Arvanitakis M, Ockenga J, Bezmarevic M, Gianotti L, Krznaric Z, Lobo DN, et al. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. Clin Nutr 2020;39:612–31.
[7] Bischoff SC, Singer P, Koller M, Barazzoni R, Cederholm T, van Gossum A. Standard operating procedures for ESPEN guidelines and consensus papers. Clin Nutr 2015;34:1043–51.
[8] Eckerwall GE, Tingstedt BB, Bergenzaun PE, Andersson RG. Immediate oral feeding in patients with mild acute pancreatitis is safe and may accelerate recovery–a randomized clinical study. Clin Nutr 2007;26:758–63.
[9] Wu LM, Sankaran SJ, Plank LD, Windsor JA, Petrov MS. Meta-analysis of gut barrier dysfunction in patients with acute pancreatitis. Br J Surg 2014;101:1644–56.
[10] Roberts KM, Nahikian-Nelms M, Ukleja A, Lara LF. Nutritional aspects of acute pancreatitis. Gastroenterol Clin N Am 2018;47:77–94.
[11] Sobral-Oliveira MB, Faintuch J, Guarita DR, Oliveira CP, Carrilho FJ. Nutritional profile of asymptomatic alcoholic patients. Arq Gastroenterol 2011;48:112–8.
[12] Kondrup J, Rasmussen HH, Hamberg O, Stanga Z, Ad Hoc EWG. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr 2003;22:321–36.
[13] Guerra RS, Fonseca I, Sousa AS, Jesus A, Pichel F, Amaral TF. ESPEN diagnostic criteria for malnutrition - a validation study in hospitalized patients. Clin Nutr 2017;36:1326–32.
[14] Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017;36:49–64.
[15] Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition - a consensus report from the global clinical nutrition community. Clin Nutr 2018;38:1–9.
[16] McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: society of critical care medicine (SCCM) and American society for parenteral and enteral nutrition (A.S.P.E.N.). J Parenter Enter Nutr 2016;40:159–211.
[17] Knudsen AW, Naver A, Bisgaard K, Nordgaard-Lassen I, Becker U, Krag A, et al. Nutrition impact symptoms, handgrip strength and nutritional risk in hospitalized patients with gastroenterological and liver diseases. Scand J Gastroenterol 2015;50:1191–8.
[18] Khatua B, El-Kurdi B, Singh VP. Obesity and pancreatitis. Curr Opin Gastroenterol 2017;33:374–82.
[19] Teich N, Aghdassi A, Fischer J, Walz B, Caca K, Wallochny T, et al. Optimal timing of oral refeeding in mild acute pancreatitis: results of an open randomized multicenter trial. Pancreas 2010;39:1088–92.
[20] Zhao XL, Zhu SF, Xue GJ, Li J, Liu YL, Wan MH, et al. Early oral refeeding based on hunger in moderate and severe acute pancreatitis: a prospective controlled, randomized clinical trial. Nutrition 2015;31:171–5.
[21] Li J, Xue GJ, Liu YL, Javed MA, Zhao XL, Wan MH, et al. Early oral refeeding wisdom in patients with mild acute pancreatitis. Pancreas 2013;42:88–91.
[22] Larino-Noia J, Lindkvist B, Iglesias-Garcia J, Seijo-Rios S, Iglesias-Canle J, Dominguez-Munoz JE. Early and/or immediately full caloric diet versus standard refeeding in mild acute pancreatitis: a randomized open-label trial. Pancreatology 2014;14:167–73.
[23] Sathiaraj E, Murthy S, Mansard MJ, Rao GV, Mahukar S, Reddy DN. Clinical trial: oral feeding with a soft diet compared with clear liquid diet as initial meal in mild acute pancreatitis. Aliment Pharmacol Ther 2008;28:777–81.
[24] Moraes JM, Felga GE, Chebli LA, Franco MB, Gomes CA, Gaburri PD, et al. A full solid diet as the initial meal in mild acute pancreatitis is safe and result in a shorter length of hospitalization: results from a prospective, randomized, controlled, double-blind clinical trial. J Clin Gastroenterol 2010;44:517–22.
[25] Horibe M, Nishizawa T, Suzuki H, Minami K, Yahagi N, Iwasaki E, et al. Timing of oral refeeding in acute pancreatitis: a systematic review and meta-analysis. United European Gastroenterol J 2016;4:725–32.
[26] Bevan MG, Asrani VM, Bharmal S, Wu LM, Windsor JA, Petrov MS. Incidence and predictors of oral feeding intolerance in acute pancreatitis: a systematic review, meta-analysis, and meta-regression. Clin Nutr 2017;36:722–9.
[27] Adiamah A, Psaltis E, Crook M, Lobo DN. A systematic review of the epidemiology, pathophysiology and current management of hyperlipidaemic pancreatitis. Clin Nutr 2018;37:1810–22.
[28] Valdivielso P, Ramirez-Bueno A, Ewald N. Current knowledge of hypertriglyceridemic pancreatitis. Eur J Intern Med 2014;25:689–94.
[29] Carr RA, Rejowski BJ, Cote GA, Pitt HA, Zyromski NJ. Systematic review of hypertriglyceridemia-induced acute pancreatitis: a more virulent etiology? Pancreatology 2016;16:469–76.
[30] Marik PE, Zaloga GP. Meta-analysis of parenteral nutrition versus enteral nutrition in patients with acute pancreatitis. BMJ 2004;328:1407.
[31] Petrov MS, van Santvoort HC, Besselink MG, van der Heijden GJ, Windsor JA, Gooszen HG. Enteral nutrition and the risk of mortality and infectious complications in patients with severe acute pancreatitis: a meta-analysis of randomized trials. Arch Surg 2008;143:1111–7.
[32] Petrov MS, Pylypchuk RD, Emelyanov NV. Systematic review: nutritional support in acute pancreatitis. Aliment Pharmacol Ther 2008;28:704–12.
[33] Cao Y, Xu Y, Lu T, Gao F, Mo Z. Meta-analysis of enteral nutrition versus total parenteral nutrition in patients with severe acute pancreatitis. Ann Nutr Metab 2008;53:268–75.
[34] Al-Omran M, Albalawi ZH, Tashkandi MF, Al-Ansary LA. Enteral versus parenteral nutrition for acute pancreatitis. Cochrane Database Syst Rev 2010:CD002837.
[35] Petrov MS, Whelan K. Comparison of complications attributable to enteral and parenteral nutrition in predicted severe acute pancreatitis: a systematic review and meta-analysis. Br J Nutr 2010;103:1287–95.
[36] Quan H, Wang X, Guo C. A meta-analysis of enteral nutrition and total parenteral nutrition in patients with acute pancreatitis. Gastroenterol Res Pract 2011;2011:698248.

[37] Yi F, Ge L, Zhao J, Lei Y, Zhou F, Chen Z, et al. Meta-analysis: total parenteral nutrition versus total enteral nutrition in predicted severe acute pancreatitis. Intern Med 2012;51:523–30.
[38] Yao H, He C, Deng L, Liao G. Enteral versus parenteral nutrition in critically ill patients with severe pancreatitis: a meta-analysis. Eur J Clin Nutr 2018;72:66–8.
[39] Li W, Liu J, Zhao S, Li J. Safety and efficacy of total parenteral nutrition versus total enteral nutrition for patients with severe acute pancreatitis: a meta-analysis. J Int Med Res 2018;46:3948–58.
[40] Wu P, Li L, Sun W. Efficacy comparisons of enteral nutrition and parenteral nutrition in patients with severe acute pancreatitis: a meta-analysis from randomized controlled trials. Biosci Rep 2018;38.
[41] Qi D, Yu B, Huang J, Peng M. Meta-analysis of early enteral nutrition provided within 24 hours of admission on clinical outcomes in acute pancreatitis. J Parenter Enter Nutr 2018;42:1139–47.
[42] Bakker OJ, van Brunschot S, Farre A, Johnson CD, Kalfarentzos F, Louie BE, et al. Timing of enteral nutrition in acute pancreatitis: meta-analysis of individuals using a single-arm of randomised trials. Pancreatology 2014;14:340–6.
[43] Bakker OJ, van Brunschot S, van Santvoort HC, Besselink MG, Bollen TL, Boermeester MA, et al. Early versus on-demand nasoenteric tube feeding in acute pancreatitis. N Engl J Med 2014;371:1983–93.
[44] Song J, Zhong Y, Lu X, Kang X, Wang Y, Guo W, et al. Enteral nutrition provided within 48 hours after admission in severe acute pancreatitis: a systematic review and meta-analysis. Medicine (Baltim) 2018;97:e11871.
[45] Petrov MS, Pylypchuk RD, Uchugina AF. A systematic review on the timing of artificial nutrition in acute pancreatitis. Br J Nutr 2009;101:787–93.
[46] Feng P, He C, Liao G, Chen Y. Early enteral nutrition versus delayed enteral nutrition in acute pancreatitis: a PRISMA-compliant systematic review and meta-analysis. Medicine (Baltim) 2017;96:e8648.
[47] Stimac D, Poropat G, Hauser G, Licul V, Franjic N, Valkovic Zujic P, et al. Early nasojejunal tube feeding versus nil-by-mouth in acute pancreatitis: a randomized clinical trial. Pancreatology 2016;16:523–8.
[48] Jin M, Zhang H, Lu B, Li Y, Wu D, Qian J, et al. The optimal timing of enteral nutrition and its effect on the prognosis of acute pancreatitis: a propensity score matched cohort study. Pancreatology 2017;17:651–7.
[49] Tiengou LE, Gloro R, Pouzoulet J, Bouhier K, Read MH, Arnaud-Battandier F, et al. Semi-elemental formula or polymeric formula: is there a better choice for enteral nutrition in acute pancreatitis? Randomized comparative study. J Parenter Enter Nutr 2006;30:1–5.
[50] Petrov MS, Loveday BP, Pylypchuk RD, McIlroy K, Phillips AR, Windsor JA. Systematic review and meta-analysis of enteral nutrition formulations in acute pancreatitis. Br J Surg 2009;96:1243–52.
[51] Poropat G, Giljaca V, Hauser G, Stimac D. Enteral nutrition formulations for acute pancreatitis. Cochrane Database Syst Rev 2015:CD010605.
[52] Eatock FC, Chong P, Menezes N, Murray L, McKay CJ, Carter CR, et al. A randomized study of early nasogastric versus nasojejunal feeding in severe acute pancreatitis. Am J Gastroenterol 2005;100:432–9.
[53] Kumar A, Singh N, Prakash S, Saraya A, Joshi YK. Early enteral nutrition in severe acute pancreatitis: a prospective randomized controlled trial comparing nasojejunal and nasogastric routes. J Clin Gastroenterol 2006;40:431–4.
[54] Singh N, Sharma B, Sharma M, Sachdev V, Bhardwaj P, Mani K, et al. Evaluation of early enteral feeding through nasogastric and nasojejunal tube in severe acute pancreatitis: a noninferiority randomized controlled trial. Pancreas 2012;41:153–9.
[55] Petrov MS, Correia MI, Windsor JA. Nasogastric tube feeding in predicted severe acute pancreatitis. A systematic review of the literature to determine safety and tolerance. JOP 2008;9:440–8.
[56] Nally DM, Kelly EG, Clarke M, Ridgway P. Nasogastric nutrition is efficacious in severe acute pancreatitis: a systematic review and meta-analysis. Br J Nutr 2014;112:1769–78.
[57] Chang YS, Fu HQ, Xiao YM, Liu JC. Nasogastric or nasojejunal feeding in predicted severe acute pancreatitis: a meta-analysis. Crit Care 2013;17:R118.
[58] Zhu Y, Yin H, Zhang R, Ye X, Wei J. Nasogastric nutrition versus nasojejunal nutrition in patients with severe acute pancreatitis: a meta-analysis of randomized controlled trials. Gastroenterol Res Pract 2016;2016:6430632.
[59] Smit M, Buddingh KT, Bosma B, Nieuwenhuijs VB, Hofker HS, Zijlstra JG. Abdominal compartment syndrome and intra-abdominal ischemia in patients with severe acute pancreatitis. World J Surg 2016;40:1454–61.
[60] Jeurnink SM, Nijs MM, Prins HA, Greving JP, Siersema PD. Antioxidants as a treatment for acute pancreatitis: a meta-analysis. Pancreatology 2015;15:203–8.
[61] Moggia E, Koti R, Belgaumkar AP, Fazio F, Pereira SP, Davidson BR, et al. Pharmacological interventions for acute pancreatitis. Cochrane Database Syst Rev 2017;4:CD011384.
[62] Asrani V, Chang WK, Dong Z, Hardy G, Windsor JA, Petrov MS. Glutamine supplementation in acute pancreatitis: a meta-analysis of randomized controlled trials. Pancreatology 2013;13:468–74.
[63] Yong L, Lu QP, Liu SH, Fan H. Efficacy of glutamine-enriched nutrition support for patients with severe acute pancreatitis: a meta-analysis. J Parenter Enter Nutr 2016;40:83–94.
[64] Jafari T, Feizi A, Askari G, Fallah AA. Parenteral immunonutrition in patients with acute pancreatitis: a systematic review and meta-analysis. Clin Nutr 2015;34:35–43.
[65] Gou S, Yang Z, Liu T, Wu H, Wang C. Use of probiotics in the treatment of severe acute pancreatitis: a systematic review and meta-analysis of randomized controlled trials. Crit Care 2014;18:R57.
[66] Besselink MG, van Santvoort HC, van der Heijden GJ, Buskens E, Gooszen HG. Dutch Acute Pancreatitis Study G. New randomized trial of probiotics in pancreatitis needed? Caution advised. Langenbeck's Arch Surg 2009;394:191–2. author reply 3-4.
[67] Kahl S, Schutte K, Glasbrenner B, Mayerle J, Simon P, Henniges F, et al. The effect of oral pancreatic enzyme supplementation on the course and outcome of acute pancreatitis: a randomized, double-blind parallel-group study. JOP 2014;15:165–74.
[68] Patankar RV, Chand R, Johnson CD. Pancreatic enzyme supplementation in acute pancreatitis. HPB Surg 1995;8:159–62.
[69] Talukdar R, Bhattacharrya A, Rao B, Sharma M, Nageshwar Reddy D. Clinical utility of the revised Atlanta classification of acute pancreatitis in a prospective cohort: have all loose ends been tied? Pancreatology 2014;14:257–62.
[70] van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med 2010;362:1491–502.
[71] van Brunschot S, Hollemans RA, Bakker OJ, Besselink MG, Baron TH, Beger HG, et al. Minimally invasive and endoscopic versus open necrosectomy for necrotising pancreatitis: a pooled analysis of individual data for 1980 patients. Gut 2018;67:697–706.
[72] van Brunschot S, van Grinsven J, van Santvoort HC, Bakker OJ, Besselink MG, Boermeester MA, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet 2018;391:51–8.
[73] Marvin RG, McKinley BA, McQuiggan M, Cocanour CS, Moore FA. Nonocclusive bowel necrosis occurring in critically ill trauma patients receiving enteral nutrition manifests no reliable clinical signs for early detection. Am J Surg 2000;179:7–12.
[74] Reintam Blaser A, Starkopf J, Alhazzani W, Berger MM, Casaer MP, Deane AM, et al. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. Intensive Care Med 2017;43:380–98.
[75] Marcos-Neira P, Zubia-Olaskoaga F, Lopez-Cuenca S, Bordeje-Laguna L. Epidemiology of Acute Pancreatitis in Intensive Care Medicine study g. Relationship between intra-abdominal hypertension, outcome and the revised Atlanta and determinant-based classifications in acute pancreatitis. BJS Open 2017;1:175–81.
[76] Sun JK, Li WQ, Ke L, Tong ZH, Ni HB, Li G, et al. Early enteral nutrition prevents intra-abdominal hypertension and reduces the severity of severe acute pancreatitis compared with delayed enteral nutrition: a prospective pilot study. World J Surg 2013;37:2053–60.
[77] Reintam Blaser A, Malbrain M, Regli A. Abdominal pressure and gastrointestinal function: an inseparable couple? Anaesthesiol Intensive Ther 2017;49:146–58.
[78] van Brunschot S, Schut AJ, Bouwense SA, Besselink MG, Bakker OJ, van Goor H, et al. Abdominal compartment syndrome in acute pancreatitis: a systematic review. Pancreas 2014;43:665–74.
[79] Tsuei BJ, Magnuson B, Swintosky M, Flynn J, Boulanger BR, Ochoa JB, et al. Enteral nutrition in patients with an open peritoneal cavity. Nutr Clin Pract 2003;18:253–8.
[80] Cothren CC, Moore EE, Ciesla DJ, Johnson JL, Moore JB, Haenel JB, et al. Postinjury abdominal compartment syndrome does not preclude early enteral feeding after definitive closure. Am J Surg 2004;188:653–8.
[81] Byrnes MC, Reicks P, Irwin E. Early enteral nutrition can be successfully implemented in trauma patients with an "open abdomen". Am J Surg 2010;199:359–62. ; discussion 63.
[82] Burlew CC, Moore EE, Cuschieri J, Jurkovich GJ, Codner P, Nirula R, et al. Who should we feed? Western Trauma Association multi-institutional study of enteral nutrition in the open abdomen after injury. J Trauma Acute Care Surg 2012;73:1380–7. ; discussion 7-8.
[83] Collier B, Guillamondegui O, Cotton B, Donahue R, Conrad A, Groh K, et al. Feeding the open abdomen. J Parenter Enter Nutr 2007;31:410–5.
[84] Dissanaike S, Pham T, Shalhub S, Warner K, Hennessy L, Moore EE, et al. Effect of immediate enteral feeding on trauma patients with an open abdomen: protection from nosocomial infections. J Am Coll Surg 2008;207:690–7.
[85] Hao L, Wang LS, Liu Y, Wang T, Guo HL, Pan J, et al. The different course of alcoholic and idiopathic chronic pancreatitis: a long-term study of 2,037 patients. PLoS One 2018;13:e0198365.
[86] Ewald N, Hardt PD. Diagnosis and treatment of diabetes mellitus in chronic pancreatitis. World J Gastroenterol 2013;19:7276–81.
[87] Meier R, Ockenga J, Pertkiewicz M, Pap A, Milinic N, Macfie J, et al. ESPEN guidelines on enteral nutrition: pancreas. Clin Nutr 2006;25:275–84.
[88] Gianotti L, Meier R, Lobo DN, Bassi C, Dejong CH, Ockenga J, et al. ESPEN guidelines on parenteral nutrition: pancreas. Clin Nutr 2009;28:428–35.
[89] Min M, Patel B, Han S, Bocelli L, Kheder J, Vaze A, et al. Exocrine pancreatic insufficiency and malnutrition in chronic pancreatitis: identification, treatment, and consequences. Pancreas 2018;47:1015–8.
[90] Olesen SS, Frandsen LK, Poulsen JL, Vestergaard P, Rasmussen HH, Drewes AM. The prevalence of underweight is increased in chronic pancreatitis outpatients and associates with reduced life quality. Nutrition 2017;43–44:1–7.

[91] Duggan SN, Smyth ND, O'Sullivan M, Feehan S, Ridgway PF, Conlon KC. The prevalence of malnutrition and fat-soluble vitamin deficiencies in chronic pancreatitis. Nutr Clin Pract 2014;29:348–54.
[92] Wehler M, Nichterlein R, Fischer B, Farnbacher M, Reulbach U, Hahn EG, et al. Factors associated with health-related quality of life in chronic pancreatitis. Am J Gastroenterol 2004;99:138–46.
[93] Olesen SS, Buyukuslu A, Kohler M, Rasmussen HH, Drewes AM. Sarcopenia associates with increased hospitalization rates and reduced survival in patients with chronic pancreatitis. Pancreatology 2019;19:245–51.
[94] Sikkens EC, Cahen DL, Koch AD, Braat H, Poley JW, Kuipers EJ, et al. The prevalence of fat-soluble vitamin deficiencies and a decreased bone mass in patients with chronic pancreatitis. Pancreatology 2013;13:238–42.
[95] Sikkens EC, Cahen DL, van Eijck C, Kuipers EJ, Bruno MJ. Patients with exocrine insufficiency due to chronic pancreatitis are undertreated: a Dutch national survey. Pancreatology 2012;12:71–3.
[96] Fernandez M, Arvanitakis M, Musala C, Deviere J, Van Steenbergen W, Putzeys V, et al. The Belgian national registry on chronic pancreatitis: a prospective multi-centre study covering more than 800 patients in one year. Pancreatology 2017;17:572–9.
[97] Hebuterne X, Hastier P, Peroux JL, Zeboudj N, Delmont JP, Rampal P. Resting energy expenditure in patients with alcoholic chronic pancreatitis. Dig Dis Sci 1996;41:533–9.
[98] Lindkvist B, Phillips ME, Dominguez-Munoz JE. Clinical, anthropometric and laboratory nutritional markers of pancreatic exocrine insufficiency: prevalence and diagnostic use. Pancreatology 2015;15:589–97.
[99] Dominguez-Munoz JE, Phillips M. Nutritional therapy in chronic pancreatitis. Gastroenterol Clin N Am 2018;47:95–106.
[100] Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P, et al. ESPEN guidelines on enteral nutrition: surgery including organ transplantation. Clin Nutr 2006;25:224–44.
[101] Sanford DE, Sanford AM, Fields RC, Hawkins WG, Strasberg SM, Linehan DC. Severe nutritional risk predicts decreased long-term survival in geriatric patients undergoing pancreaticoduodenectomy for benign disease. J Am Coll Surg 2014;219:1149–56.
[102] Schnelldorfer T, Adams DB. The effect of malnutrition on morbidity after Surgery for chronic pancreatitis. Am Surg 2005;71:466–72. ; discussion 72-3.
[103] Singh S, Midha S, Singh N, Joshi YK, Garg PK. Dietary counseling versus dietary supplements for malnutrition in chronic pancreatitis: a randomized controlled trial. Clin Gastroenterol Hepatol 2008;6:353–9.
[104] Dutta SK, Bustin MP, Russell RM, Costa BS. Deficiency of fat-soluble vitamins in treated patients with pancreatic insufficiency. Ann Intern Med 1982;97:549–52.
[105] Cheshire J, Kolli S. Vitamin A deficiency due to chronic malabsorption: an ophthalmic manifestation of a systemic condition. BMJ Case Rep 2017;2017.
[106] Livingstone C, Davis J, Marvin V, Morton K. Vitamin A deficiency presenting as night blindness during pregnancy. Ann Clin Biochem 2003;40:292–4.
[107] Tran TC, van Lanschot JJ, Bruno MJ, van Eijck CH. Functional changes after pancreatoduodenectomy: diagnosis and treatment. Pancreatology 2009;9:729–37.
[108] de la Iglesia-Garcia D, Huang W, Szatmary P, Baston-Rey I, Gonzalez-Lopez J, Prada-Ramallal G, et al. Efficacy of pancreatic enzyme replacement therapy in chronic pancreatitis: systematic review and meta-analysis. Gut 2017;66:1354–5.
[109] Dominguez-Munoz JE, Iglesias-Garcia J. Oral pancreatic enzyme substitution therapy in chronic pancreatitis: is clinical response an appropriate marker for evaluation of therapeutic efficacy? JOP 2010;11:158–62.
[110] Duggan S, O'Sullivan M, Feehan S, Ridgway P, Conlon K. Nutrition treatment of deficiency and malnutrition in chronic pancreatitis: a review. Nutr Clin Pract 2010;25:362–70.
[111] Sikkens EC, Cahen DL, van Eijck C, Kuipers EJ, Bruno MJ. The daily practice of pancreatic enzyme replacement therapy after pancreatic surgery: a northern European survey: enzyme replacement after surgery. J Gastrointest Surg 2012;16:1487–92.
[112] Gooden HM, White KJ. Pancreatic cancer and supportive care–pancreatic exocrine insufficiency negatively impacts on quality of life. Support Care Cancer 2013;21:1835–41.
[113] Bachmann K, Tomkoetter L, Kutup A, Erbes J, Vashist Y, Mann O, et al. Is the Whipple procedure harmful for long-term outcome in treatment of chronic pancreatitis? 15-years follow-up comparing the outcome after pylorus-preserving pancreatoduodenectomy and Frey procedure in chronic pancreatitis. Ann Surg 2013;258:815–20. ; discussion 20-1.
[114] Lindkvist B, Dominguez-Munoz JE, Luaces-Regueira M, Castineiras-Alvarino M, Nieto-Garcia L, Iglesias-Garcia J. Serum nutritional markers for prediction of pancreatic exocrine insufficiency in chronic pancreatitis. Pancreatology 2012;12:305–10.
[115] Regan PT, Malagelada JR, DiMagno EP, Glanzman SL, Go VL. Comparative effects of antacids, cimetidine and enteric coating on the therapeutic response to oral enzymes in severe pancreatic insufficiency. N Engl J Med 1977;297:854–8.
[116] Layer P, von der Ohe MR, Holst JJ, Jansen JB, Grandt D, Holtmann G, et al. Altered postprandial motility in chronic pancreatitis: role of malabsorption. Gastroenterology 1997;112:1624–34.
[117] Wooldridge JL, Heubi JE, Amaro-Galvez R, Boas SR, Blake KV, Nasr SZ, et al. EUR-1008 pancreatic enzyme replacement is safe and effective in patients with cystic fibrosis and pancreatic insufficiency. J Cyst Fibros 2009;8:405–17.
[118] Haaber AB, Rosenfalck AM, Hansen B, Hilsted J, Larsen S. Bone mineral metabolism, bone mineral density, and body composition in patients with chronic pancreatitis and pancreatic exocrine insufficiency. Int J Pancreatol 2000;27:21–7.
[119] Kalvaria I, Labadarios D, Shephard GS, Visser L. Marks IN. Biochemical vitamin E deficiency in chronic pancreatitis. Int J Pancreatol 1986;1:119–28.
[120] Mann ST, Stracke H, Lange U, Klor HU, Teichmann J. Alterations of bone mineral density and bone metabolism in patients with various grades of chronic pancreatitis. Metabolism 2003;52:579–85.
[121] Haas S, Krins S, Knauerhase A, Lohr M. Altered bone metabolism and bone density in patients with chronic pancreatitis and pancreatic exocrine insufficiency. JOP 2015;16:58–62.
[122] Gan KH, Geus WP, Bakker W, Lamers CB, Heijerman HG. In vitro dissolution profiles of enteric-coated microsphere/microtablet pancreatin preparations at different pH values. Aliment Pharmacol Ther 1996;10:771–5.
[123] Lohr JM, Hummel FM, Pirilis KT, Steinkamp G, Korner A, Henniges F. Properties of different pancreatin preparations used in pancreatic exocrine insufficiency. Eur J Gastroenterol Hepatol 2009;21:1024–31.
[124] DiMagno EP, Malagelada JR, Go VL, Moertel CG. Fate of orally ingested enzymes in pancreatic insufficiency. Comparison of two dosage schedules. N Engl J Med 1977;296:1318–22.
[125] D'Haese JG, Ceyhan GO, Demir IE, Layer P, Uhl W, Lohr M, et al. Pancreatic enzyme replacement therapy in patients with exocrine pancreatic insufficiency due to chronic pancreatitis: a 1-year disease management study on symptom control and quality of life. Pancreas 2014;43:834–41.
[126] Ramesh H, Reddy N, Bhatia S, Rajkumar JS, Bapaye A, Kini D, et al. A 51-week, open-label clinical trial in India to assess the efficacy and safety of pancreatin 40000 enteric-coated minimicrospheres in patients with pancreatic exocrine insufficiency due to chronic pancreatitis. Pancreatology 2013;13:133–9.
[127] Thorat V, Reddy N, Bhatia S, Bapaye A, Rajkumar JS, Kini DD, et al. Randomised clinical trial: the efficacy and safety of pancreatin enteric-coated minimicrospheres (Creon 40000 MMS) in patients with pancreatic exocrine insufficiency due to chronic pancreatitis–a double-blind, placebo-controlled study. Aliment Pharmacol Ther 2012;36:426–36.
[128] Whitcomb DC, Lehman GA, Vasileva G, Malecka-Panas E, Gubergrits N, Shen Y, et al. Pancrelipase delayed-release capsules (CREON) for exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatic surgery: a double-blind randomized trial. Am J Gastroenterol 2010;105:2276–86.
[129] Somaraju UR, Solis-Moya A. Pancreatic enzyme replacement therapy for people with cystic fibrosis. Cochrane Database Syst Rev 2014:CD008227.
[130] Bruno MJ, Borm JJ, Hoek FJ, Delzenne B, Hofmann AF, de Goeij JJ, et al. Gastric transit and pharmacodynamics of a two-millimeter enteric-coated pancreatin microsphere preparation in patients with chronic pancreatitis. Dig Dis Sci 1998;43:203–13.
[131] Taylor CJ, Thieroff-Ekerdt R, Shiff S, Magnus L, Fleming R, Gommoll C. Comparison of two pancreatic enzyme products for exocrine insufficiency in patients with cystic fibrosis. J Cyst Fibros 2016;15:675–80.
[132] Dominguez-Munoz JE, Iglesias-Garcia J, Iglesias-Rey M, Figueiras A, Vilarino-Insua M. Effect of the administration schedule on the therapeutic efficacy of oral pancreatic enzyme supplements in patients with exocrine pancreatic insufficiency: a randomized, three-way crossover study. Aliment Pharmacol Ther 2005;21:993–1000.
[133] Keller J, Layer P. Human pancreatic exocrine response to nutrients in health and disease. Gut 2005;54(Suppl 6):vi1–28.
[134] Safdi M, Bekal PK, Martin S, Saeed ZA, Burton F, Toskes PP. The effects of oral pancreatic enzymes (Creon 10 capsule) on steatorrhea: a multicenter, placebo-controlled, parallel group trial in subjects with chronic pancreatitis. Pancreas 2006;33:156–62.
[135] O'Keefe SJ, Cariem AK, Levy M. The exacerbation of pancreatic endocrine dysfunction by potent pancreatic exocrine supplements in patients with chronic pancreatitis. J Clin Gastroenterol 2001;32:319–23.
[136] Halm U, Loser C, Lohr M, Katschinski M, Mossner J. A double-blind, randomized, multicentre, crossover study to prove equivalence of pancreatin minimicrospheres versus microspheres in exocrine pancreatic insufficiency. Aliment Pharmacol Ther 1999;13:951–7.
[137] Opekun Jr AR, Sutton Jr FM, Graham DY. Lack of dose-response with Pancrease MT for the treatment of exocrine pancreatic insufficiency in adults. Aliment Pharmacol Ther 1997;11:981–6.
[138] Vecht J, Symersky T, Lamers CB, Masclee AA. Efficacy of lower than standard doses of pancreatic enzyme supplementation therapy during acid inhibition in patients with pancreatic exocrine insufficiency. J Clin Gastroenterol 2006;40:721–5.
[139] FitzSimmons SC, Burkhart GA, Borowitz D, Grand RJ, Hammerstrom T, Durie PR, et al. High-dose pancreatic-enzyme supplements and fibrosing colonopathy in children with cystic fibrosis. N Engl J Med 1997;336:1283–9.
[140] Ferrie S, Graham C, Hoyle M. Pancreatic enzyme supplementation for patients receiving enteral feeds. Nutr Clin Pract 2011;26:349–51.
[141] Gubergrits N, Malecka-Panas E, Lehman GA, Vasileva G, Shen Y, Sander-Struckmeier S, et al. A 6-month, open-label clinical trial of pancrelipase delayed-release capsules (Creon) in patients with exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatic surgery. Aliment Pharmacol Ther 2011;33:1152–61.

[142] Phillips ME. Pancreatic exocrine insufficiency following pancreatic resection. Pancreatology 2015;15:449–55.
[143] Dominguez-Munoz JE, Iglesias-Garcia J, Vilarino-Insua M, Iglesias-Rey M. 13C-mixed triglyceride breath test to assess oral enzyme substitution therapy in patients with chronic pancreatitis. Clin Gastroenterol Hepatol 2007;5:484–8.
[144] Dominguez-Munoz JE, Iglesias-Garcia J, Iglesias-Rey M, Vilarino-Insua M. Optimising the therapy of exocrine pancreatic insufficiency by the association of a proton pump inhibitor to enteric coated pancreatic extracts. Gut 2006;55:1056–7.
[145] Sander-Struckmeier S, Beckmann K, Janssen-van Solingen G, Pollack P. Retrospective analysis to investigate the effect of concomitant use of gastric acid-suppressing drugs on the efficacy and safety of pancrelipase/pancreatin (CREON(R)) in patients with pancreatic exocrine insufficiency. Pancreas 2013;42:983–9.
[146] Ni Chonchubhair HM, Bashir Y, Dobson M, Ryan BM, Duggan SN, Conlon KC. The prevalence of small intestinal bacterial overgrowth in non-surgical patients with chronic pancreatitis and pancreatic exocrine insufficiency (PEI). Pancreatology 2018;18:379–85.
[147] Majumder S, Chari ST. Chronic pancreatitis. Lancet 2016;387:1957–66.
[148] Sabater L, Ausania F, Bakker OJ, Boadas J, Dominguez-Munoz JE, Falconi M, et al. Evidence-based guidelines for the management of exocrine pancreatic insufficiency after pancreatic surgery. Ann Surg 2016;264:949–58.
[149] Gianotti L, Besselink MG, Sandini M, Hackert T, Conlon K, Gerritsen A, et al. Nutritional support and therapy in pancreatic surgery: a position paper of the International Study Group on Pancreatic Surgery (ISGPS). Surgery 2018;164:1035–48.
[150] Diener MK, Rahbari NN, Fischer L, Antes G, Buchler MW, Seiler CM. Duodenum-preserving pancreatic head resection versus pancreatoduodenectomy for surgical treatment of chronic pancreatitis: a systematic review and meta-analysis. Ann Surg 2008;247:950–61.
[151] Yin Z, Sun J, Yin D, Wang J. Surgical treatment strategies in chronic pancreatitis: a meta-analysis. Arch Surg 2012;147:961–8.
[152] Diener MK, Huttner FJ, Kieser M, Knebel P, Dorr-Harim C, Distler M, et al. Partial pancreatoduodenectomy versus duodenum-preserving pancreatic head resection in chronic pancreatitis: the multicentre, randomised, controlled, double-blind ChroPac trial. Lancet 2017;390:1027–37.
[153] Zhou Y, Shi B, Wu L, Wu X, Li Y. Frey procedure for chronic pancreatitis: evidence-based assessment of short- and long-term results in comparison to pancreatoduodenectomy and Beger procedure: a meta-analysis. Pancreatology 2015;15:372–9.
[154] Bachmann K, Tomkoetter L, Erbes J, Hofmann B, Reeh M, Perez D, et al. Beger and Frey procedures for treatment of chronic pancreatitis: comparison of outcomes at 16-year follow-up. J Am Coll Surg 2014;219:208–16.
[155] Duggan SN, Smyth ND, Murphy A, Macnaughton D, O'Keefe SJ, Conlon KC. High prevalence of osteoporosis in patients with chronic pancreatitis: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2014;12:219–28.
[156] Uc A, Andersen DK, Bellin MD, Bruce JI, Drewes AM, Engelhardt JF, et al. Chronic pancreatitis in the 21st century - research challenges and opportunities: summary of a national institute of diabetes and digestive and kidney diseases workshop. Pancreas 2016;45:1365–75.
[157] Tignor AS, Wu BU, Whitlock TL, Lopez R, Repas K, Banks PA, et al. High prevalence of low-trauma fracture in chronic pancreatitis. Am J Gastroenterol 2010;105:2680–6.
[158] Bang UC, Benfield T, Bendtsen F, Hyldstrup L, Beck Jensen JE. The risk of fractures among patients with cirrhosis or chronic pancreatitis. Clin Gastroenterol Hepatol 2014;12:320–6.
[159] Expert Panel on Musculoskeletal I, Ward RJ, Roberts CC, Bencardino JT, Arnold E, Baccei SJ, et al. ACR appropriateness criteria((R)) osteoporosis and bone mineral density. J Am Coll Radiol 2017;14:S189–202.
[160] American Gastroenterological Association medical position statement: guidelines on osteoporosis in gastrointestinal diseases. Gastroenterology 2003;124:791–4.
[161] Prevention and management of osteoporosis. In: World Health Organization technical report series; 2003. p. 1–164. vol. 921 back cover.
[162] de-Madaria E, Abad-Gonzalez A, Aparicio JR, Aparisi L, Boadas J, Boix E, et al. The Spanish Pancreatic Club's recommendations for the diagnosis and treatment of chronic pancreatitis: part 2 (treatment). Pancreatology 2013;13:18–28.
[163] Delhaye M, Van Steenbergen W, Cesmeli E, Pelckmans P, Putzeys V, Roeyen G, et al. Belgian consensus on chronic pancreatitis in adults and children: statements on diagnosis and nutritional, medical, and surgical treatment. Acta Gastroenterol Belg 2014;77:47–65.
[164] Frulloni L, Falconi M, Gabbrielli A, Gaia E, Graziani R, Pezzilli R, et al. Italian consensus guidelines for chronic pancreatitis. Dig Liver Dis 2010;42(Suppl 6):S381–406.
[165] Mirtallo JM, Forbes A, McClave SA, Jensen GL, Waitzberg DL, Davies AR, et al. International consensus guidelines for nutrition therapy in pancreatitis. J Parenter Enter Nutr 2012;36:284–91.
[166] Maruki J, Sai JK, Watanabe S. Efficacy of low-fat diet against dyspepsia associated with nonalcoholic mild pancreatic disease diagnosed using the Rosemont criteria. Pancreas 2013;42:49–52.
[167] Castineira-Alvarino M, Lindkvist B, Luaces-Regueira M, Iglesias-Garcia J, Larino-Noia J, Nieto-Garcia L, et al. The role of high fat diet in the development of complications of chronic pancreatitis. Clin Nutr 2013;32:830–6.
[168] Dutta SK, Hlasko J. Dietary fiber in pancreatic disease: effect of high fiber diet on fat malabsorption in pancreatic insufficiency and in vitro study of the interaction of dietary fiber with pancreatic enzymes. Am J Clin Nutr 1985;41:517–25.
[169] Greer JB, Greer P, Sandhu BS, Alkaade S, Wilcox CM, Anderson MA, et al. Nutrition and inflammatory biomarkers in chronic pancreatitis patients. Nutr Clin Pract 2018;34:387–99.
[170] Klapdor S, Richter E, Klapdor R. Vitamin D status and per-oral vitamin D supplementation in patients suffering from chronic pancreatitis and pancreatic cancer disease. Anticancer Res 2012;32:1991–8.
[171] Caliari S, Benini L, Sembenini C, Gregori B, Carnielli V, Vantini I. Medium-chain triglyceride absorption in patients with pancreatic insufficiency. Scand J Gastroenterol 1996;31:90–4.
[172] Caliari S, Benini L, Bonfante F, Brentegani MT, Fioretta A, Vantini I. Pancreatic extracts are necessary for the absorption of elemental and polymeric enteral diets in severe pancreatic insufficiency. Scand J Gastroenterol 1993;28:749–52.
[173] Stanga Z, Giger U, Marx A, DeLegge MH. Effect of jejunal long-term feeding in chronic pancreatitis. J Parenter Enter Nutr 2005;29:12–20.
[174] Skipworth JR, Raptis DA, Wijesuriya S, Puthucheary Z, Olde Damink SW, Imber C, et al. The use of nasojejunal nutrition in patients with chronic pancreatitis. JOP 2011;12:574–80.
[175] Ridtitid W, Lehman GA, Watkins JL, McHenry L, Fogel EL, Sherman S, et al. Short- and long-term outcomes from percutaneous endoscopic gastrostomy with jejunal extension. Surg Endosc 2017;31:2901–9.
[176] O'Keefe S, Rolniak S, Raina A, Graham T, Hegazi R, Centa-Wagner P. Enteral feeding patients with gastric outlet obstruction. Nutr Clin Pract 2012;27:76–81.
[177] Silk DB. Formulation of enteral diets for use in jejunal enteral feeding. Proc Nutr Soc 2008;67:270–2.