

Long - term follow up of a simplified and less burdened pancreatic duct ligation model of exocrine pancreatic insufficiency in Goettingen Minipigs

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Abstract

Background

Pancreatic duct ligation in a minipig model leads to exocrine pancreatic insufficiency (EPI). This allows studies of digestive processes and pancreatic enzyme replacement therapies (PERT). However, detailed descriptions of the surgical procedure, perioperative management, and determination of exocrine pancreatic insufficiency are scarce in literature. To date, data of long-term health status of minipigs after induction of EPI are not available. This study describes in detail the experimental approach of EPI-induction via pancreatic duct ligation in minipigs and long-term results of the animal's health state.

Methods

14 Goettingen minipigs underwent pancreatic duct ligation via midline laparotomy for the induction of exocrine pancreatic insufficiency. Fecal fat content, fat absorption, body weight, chymotrypsin levels, blood vitamin levels and glucose levels were determined. Follow-up data was gathered for a period of 180 weeks postoperatively.

Results

Exocrine pancreatic insufficiency was successfully induced in 12 Goettingen minipigs. Fecal fat content increased from 9.0% to 30.9% ($p < 0.001$). Mean coefficient of fat absorption decreased from 90% (± 2.8) to 24.2% (± 8.3). PERT led to a significant increase of fat absorption. Two minipigs failed to develop exocrine insufficiency most likely due to undetected accessory pancreatic ducts. All animals tolerated the procedure very well and gained weight within 6 weeks past surgery. Follow up for 180 weeks showed a stable body weight and health state of the animals with normal blood glucose levels. Vitamin E and B12 levels dropped significantly between post-op week 125 and 134 requiring vitamin supplementation.

Conclusions

Pancreatic duct ligation in minipigs is an excellent method to induce exocrine pancreatic insufficiency. It is important to identify and ligate accessory pancreatic ducts since persistence of accessory ducts will lead to maintenance of exocrine pancreatic function. The EPI model caused no persistent side effects in the animals and can be applied in long-term EPI studies. However, it is important to substitute Vitamin B12 and E as their concentration drops in the long-term period.

Full Text

This preprint is available for [download as a PDF](#).

Table

Due to technical limitations, Table 1 is only available for download from the Supplementary Files section.

Figures

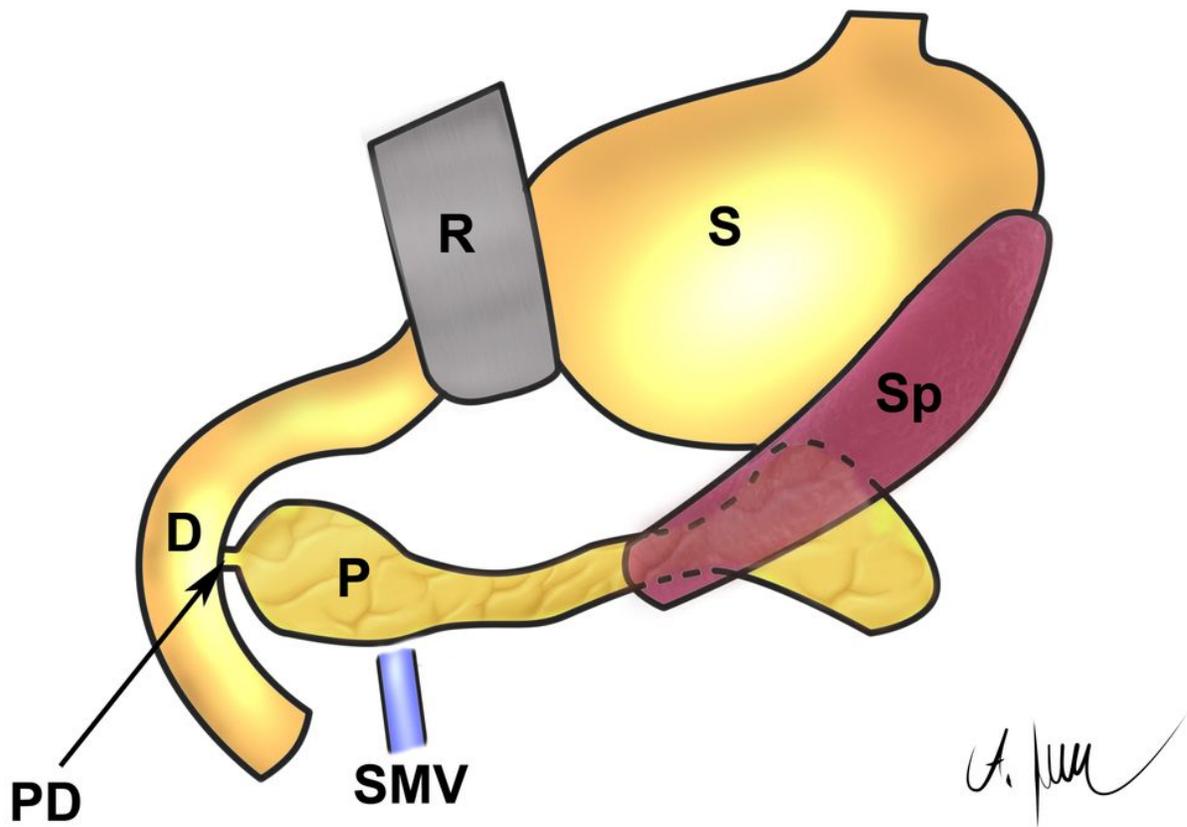


Figure 1

Schematic drawing of the upper abdomen of a Goettingen minipig. P = pancreas, PD = pancreatic duct, CBD = common bile duct draining into the duodenum separately, SP = spleen, S = stomach, R = retractor, D = duodenum, SMV = superior mesenteric vein.

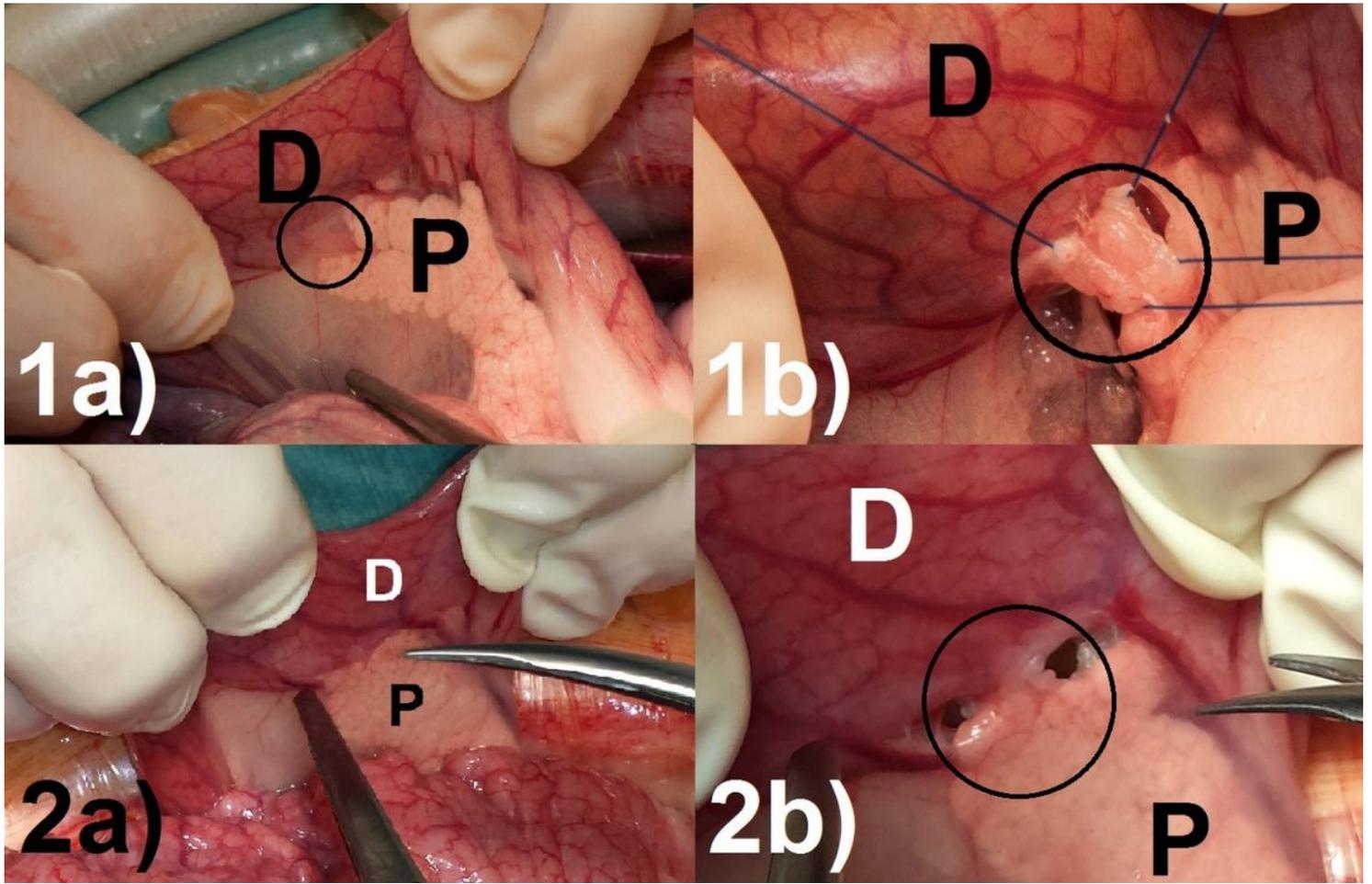


Figure 2

Intraoperative view of the pancreatic duct (encircled) embedded in a membrane between pancreas (P) and duodenum (D) prior to (1a, 2a) and after (1b, 2b) separation. The pancreatic duct is difficult to identify on image 2a.

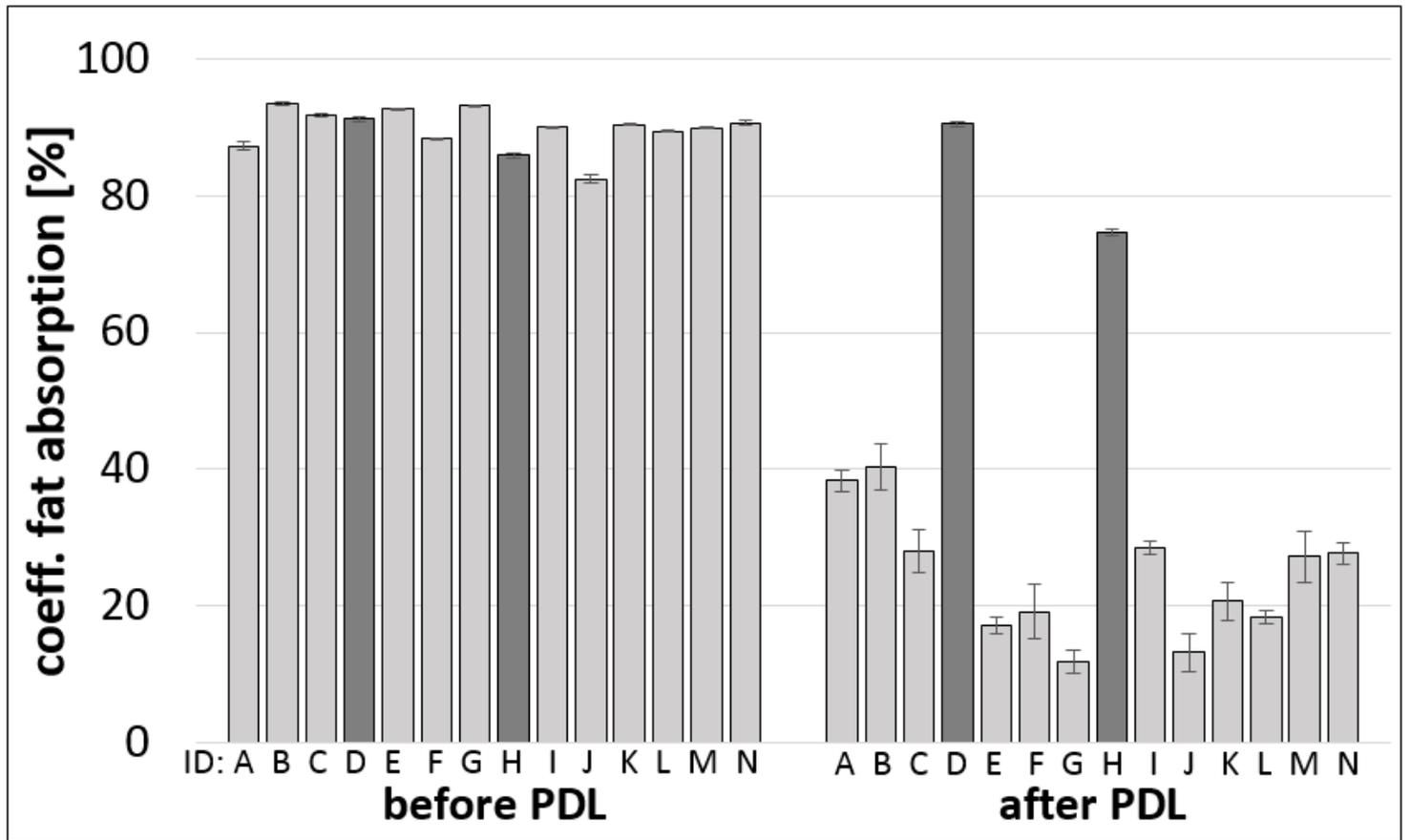


Figure 3

Coefficient of fat absorption (CFA) in minipigs before and six weeks after pancreatic duct ligation (PDL). Pigs were fed with a high-fat diet (18.5%) for seven days twice a day. Feces were collected on days 5 – 7, and fat absorption was then determined. Animal identification (ID) ranged from A to N. Dark columns indicate animals D and H with only a minor reduction in fat absorption.

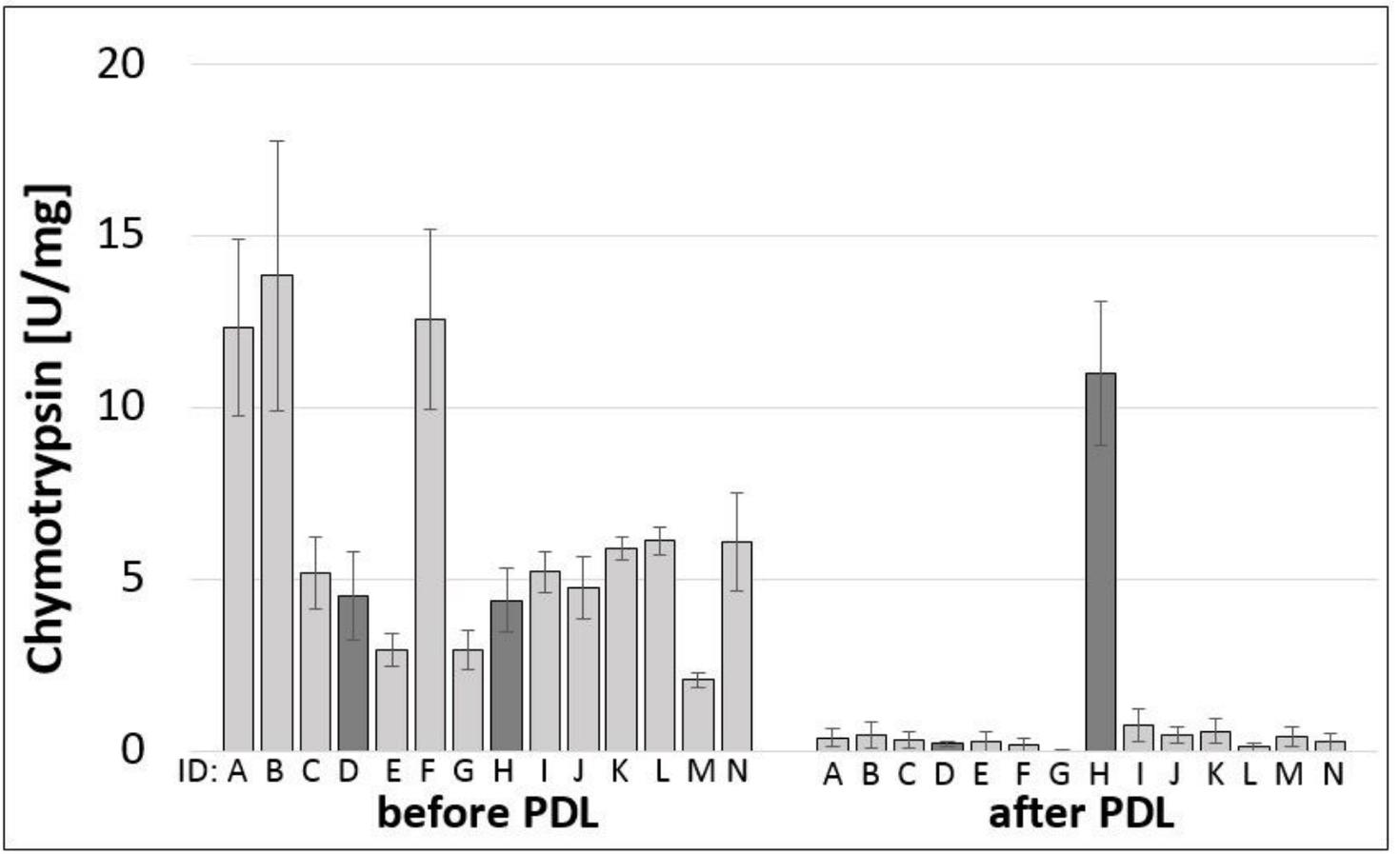


Figure 4

Fecal chymotrypsin content in minipigs before and six weeks after pancreatic duct ligation (PDL). Pigs were fed with a high-fat diet (18.5%) for seven days twice a day. Feces were collected on days 5 – 7, and chymotrypsin activity was then determined. Animal identification (ID) ranged from A to N. Dark columns mark the results of animal D with a decrease in chymotrypsin absorption and animal H with an increase after pancreatic duct ligation.

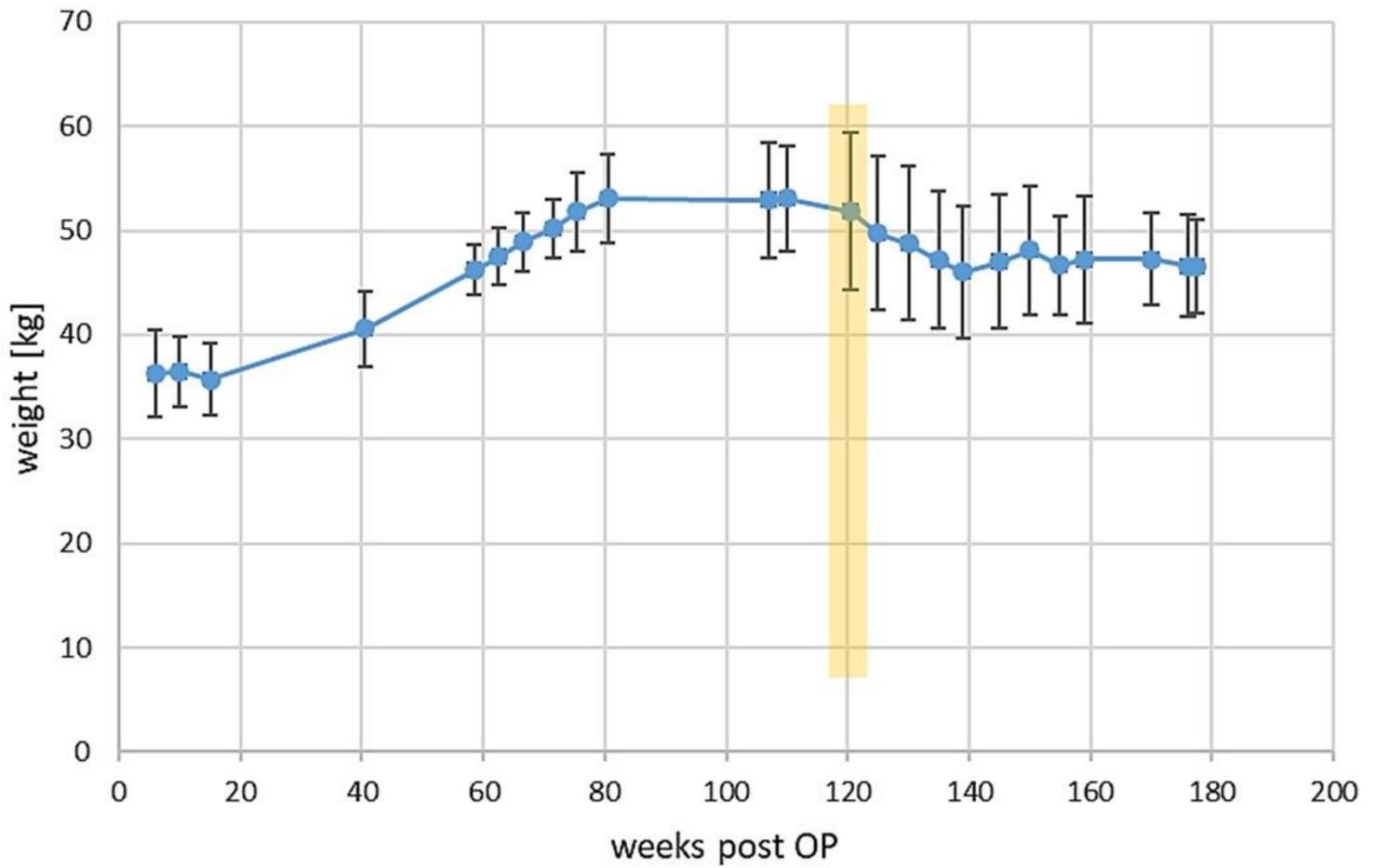


Figure 5

Body weight of pancreas duct ligated minipigs post-OP in long-term husbandry. Values are presented as mean \pm standard deviation. Yellow area marks change of fodder.

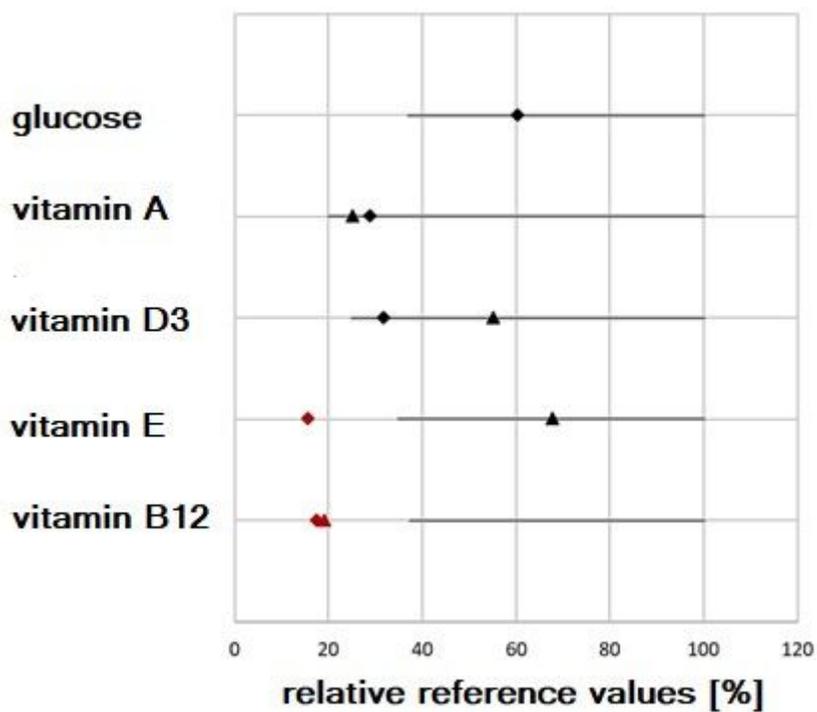


Figure 6

Blood level values of vitamins and glucose normalized to the reference values. The upper reference limit was set to 100 %. = values before supplementation (130 ± 10 weeks post OP, n= 8). = values after supplementation (155 ± 9 weeks post OP, n = 5). Red color indicates values below reference range. Although vitamin B12 levels were still below the reference range after supplementation, eating behavior has changed significantly afterwards. All values are in percent and gray lines indicate reference range.

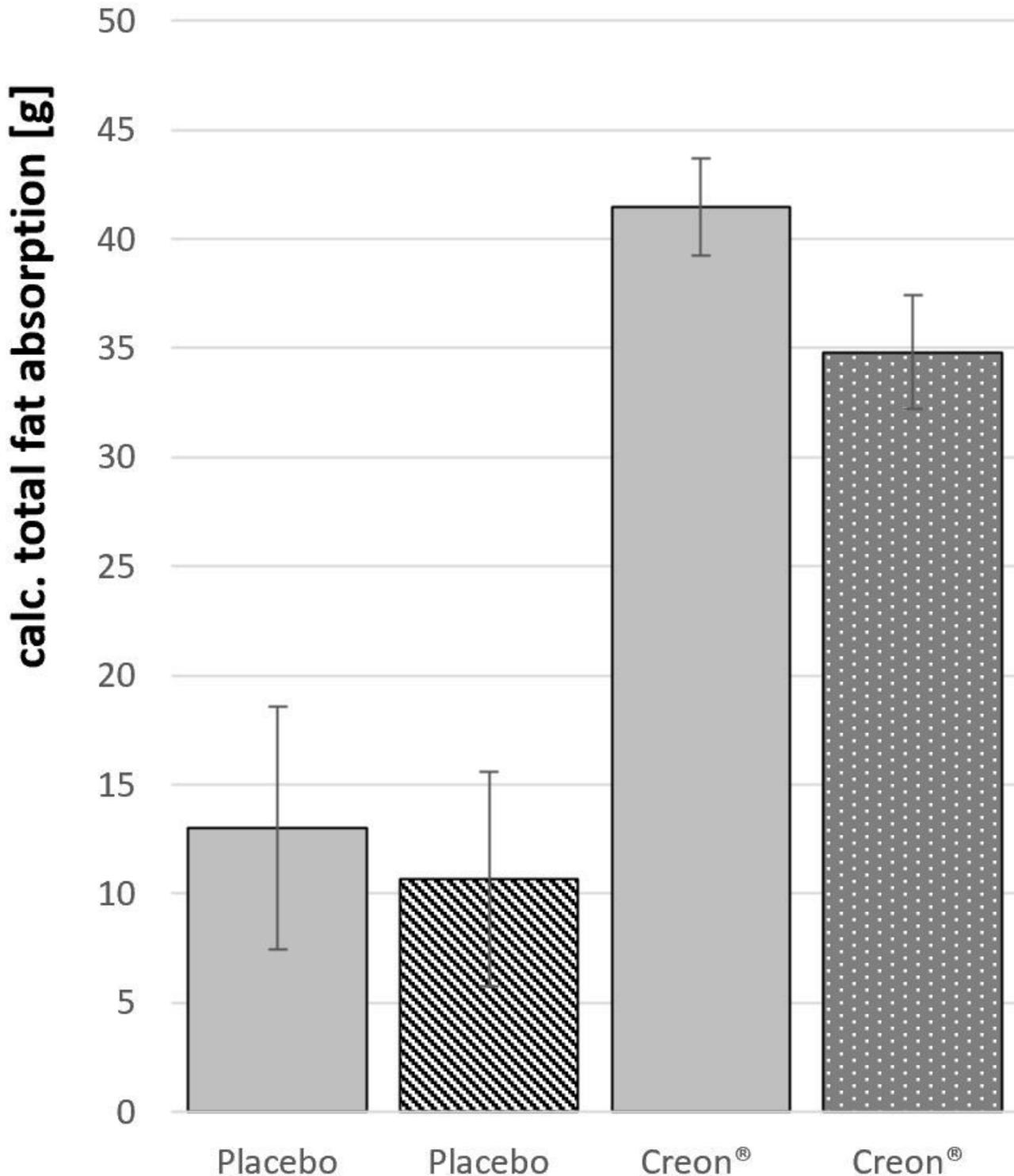


Figure 7

Total fat absorption with or without pancreatic enzyme replacement therapy (PERT) indicated by coefficient of fat absorption (CFA) six weeks (filled bar) after pancreatic duct ligation (PDL) and 97-126 weeks (dashed and dotted bars) after PDL. The diagram demonstrates the significant increase of CFA after PERT in short-term as in long-term studies.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Tab1PancreaticDuctLigationLuu.xlsx](#)
- [ARRIVEGuidelines.pdf](#)