

# Results of Treatment of Hypertriglyceridemia-induced Acute Necrotizing Pancreatitis with the Use of Plasmapheresis

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**Abstract. Introduction:** Additional risk factors have been identified, and the outcomes of surgical treatment in patients with hypertriglyceridemia-induced acute necrotizing pancreatitis treated with plasmapheresis have been analyzed.

**Aim:** To evaluate the effectiveness of plasmapheresis in the treatment of patients with hypertriglyceridemia-induced acute necrotizing pancreatitis, with an emphasis on the early use of minimally invasive techniques and delayed open surgical interventions, and to identify additional risk factors associated with adverse disease outcomes.

**Materials and methods:** The treatment outcomes of 82 patients have been analyzed: 53 patients (65%) were included in the main group, and 29 patients (35%) were included in the comparison group.

**Results:** The use of plasmapheresis resulted in a significant reduction in blood triglyceride levels ( $p=0.002$ ), total cholesterol ( $p=0.001$ ), low-density lipoproteins ( $p=0.012$ ), and the atherogenic index ( $p=0.001$ ). In the comparison group, the decrease in these parameters was not significant. In the main group, a favorable disease course and the effectiveness of minimally invasive interventions were achieved in 60% of the patients (29/48), compared with 46% (12/26) in the comparison group ( $p=0.238$ ).

**Discussion:** According to the ROC analysis, adverse prognostic factors for a complicated disease course included arterial hypertension ( $p=0.042$ ), overweight with a body mass index greater than 27.6 kg/m<sup>2</sup> ( $p=0.030$ ), diabetes mellitus ( $p=0.021$ ), and hypertriglyceridemia ( $p=0.001$ ). This study will allow us to evaluate the results of the treatment of patients with hypertriglyceride-induced acute necrotic pancreatitis and the effectiveness of plasmapheresis, as well as to identify additional prognostic risk factors leading to laparotomy.

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**Conclusions:** Plasmapheresis in the early stages of hypertriglyceride-induced acute necrotic pancreatitis had a positive effect on the course of the disease and ensured the final effectiveness of mini-invasive surgical interventions in 60% of the patients in the main group. Additional prognostic factors for complicated hypertriglyceride-induced acute necrotic pancreatitis, accompanied by purulent-septic complications and requiring laparotomy, are arterial hypertension, a body mass index greater than 27.6 (kg/m<sup>2</sup>), diabetes mellitus, and hypertriglyceridemia.

**Keywords:** hypertriglyceridemia, acute necrotizing pancreatitis, plasmapheresis, laparotomy risk factors, surgical treatment.

## Hipertrigliceridemijos sukkelto ūmaus nekrozinio pankreatito gydymo plazmaferozės metodu rezultatai

**Santrauka. Įvadas:** Nustatyti papildomi rizikos veiksniai ir išanalizuoti pacientų, sergančių hipertrigliceridemijos sukeltu ūmiu nekrozinio pankreatitu, kuriems buvo taikoma plazmaferozė, chirurginio gydymo rezultatai.

**Tikslas:** Įvertinti plazmaferozės veiksmingumą gydant pacientus, sergančius hipertrigliceridemijos sukeltu ūmiu nekrozinio pankreatitu, ypatingą dėmesį skiriant ankstyvam minimaliai invazinių metodų taikymui ir atidėtoms atviroms chirurginėms intervencijoms, bei nustatyti papildomus rizikos veiksnius, susijusius su nepalankia ligos baigtimi.

**Medžiaga ir metodai:** Išanalizuoti 82 pacientų gydymo rezultatai: 53 pacientai (65 %) buvo įtraukti į pagrindinę grupę, o 29 pacientai (35 %) – į lyginamąją grupę.

**Rezultatai:** Taikant plazmaferozę, gerokai sumažėjo trigliceridų kiekis kraujyje ( $p = 0,002$ ), bendrasis cholesterolis ( $p = 0,001$ ), mažo tankio lipoproteinų ( $p = 0,012$ ) ir aterogeninis indeksas ( $p = 0,001$ ). Lyginamosios grupės pacientų šių rodiklių sumažėjimas nebuvo reikšmingas. Pagrindinėje grupėje palanki ligos eiga ir minimaliai invazinių intervencijų veiksmingumas buvo pasiekti 60 % pacientų (29 iš 48), palyginti su 46 % (12 iš 26) lyginamojoje grupėje ( $p = 0,238$ ).

**Aptarimas:** Remiantis ROC analize, nepalankūs prognostiniai veiksniai, susiję su komplikauta ligos eiga, buvo arterinė hipertenzija ( $p = 0,042$ ), antsvoris, kai kūno masės indeksas viršijo 27,6 kg/m<sup>2</sup> ( $p = 0,030$ ), cukrinis diabetas ( $p = 0,021$ ) ir hipertrigliceridemija ( $p = 0,001$ ). Šis tyrimas leis įvertinti pacientų, sergančių hipertrigliceridemijos sukeltu ūmiu nekrozinio pankreatitu, gydymo rezultatus ir plazmaferozės veiksmingumą, taip pat nustatyti papildomus prognostinius rizikos veiksnius, lemiančius laparotomijos būtinybę.

**Išvados:** Plazmaferozė ankstyvosiose hipertrigliceridų sukeltos ūminio nekrozinio pankreatito stadijose turėjo teigiamą poveikį ligos eigai ir užtikrino galutinį minimaliai invazinių chirurginių intervencijų veiksmingumą 60 % pagrindinės grupės pacientų. Papildomi prognostiniai veiksniai, susiję su komplikotu hipertrigliceridemijos sukeltu ūmiu nekrozinio pankreatitu, kuris sukelia pūlingas septines komplikacijas ir dėl kurio būtina laparotomija, yra arterinė hipertenzija, kūno masės indeksas, didesnis nei 27,6 (kg/m<sup>2</sup>), cukrinis diabetas ir hipertrigliceridemija.

**Raktiniai žodžiai:** hipertrigliceridemija, ūmus nekrozinis pankreatitas, plazmaferozė (kraujo filtracija), laparotomijos rizikos veiksniai, chirurginis gydymas.

## Introduction

Acute Pancreatitis (AP) remains one of the most complex abdominal diseases in peacetime. Treatment of AP is accompanied by significant material costs for treating patients, which is due to the growth of necrotic forms of the disease, possible numerous purulent complications, and the development of sepsis [1,2].

The mortality rate in AP currently ranges from 4.5% to 15%. In complicated forms of the disease, it may reach 60–85%, and, in cases of fulminant necrotizing AP, which is often accompanied by multiple organ dysfunction or failure, it can approach 100%. Also of concern is the rising incidence

of AP, which has been increasing globally by 2–5% per year and varies widely, ranging from 3.4 to 73.4 cases per 100,000 population [3].

Among the causes of AP, alimentary factors (alcohol, fatty foods, etc.), as well as diseases of the extrahepatic biliary tract (primarily, cholelithiasis and its complications), maintain their relevance. *Hypertriglyceridemia* (HTG) occupies a prominent place among other established etiological factors for the AP occurrence. The latter is characterized by a blood plasma triglyceride (TG) concentration exceeding 2.0 mmol/L, along with elevated levels of chylomicrons and intermediate-density lipoprotein particles. An increase in the concentration of TG in the blood plasma can be caused by hereditary dyslipidemic anomaly – familial hyperlipidemia, familial chylomicronemic syndrome, and secondary factors – such as alcohol abuse, *Diabetes Mellitus* (DM), and pregnancy [4,5]. Hereditary hypertriglyceridemia is determined exclusively by an increase in the level of *Very Low-Density Lipoproteins* (VLDL), which is associated with endothelial dysfunction, leukocyte activation, and insulin resistance [6,7].

The relevance of HTG is due to the prevalence of its inherent conditions – such as coronary heart disease, DM, obesity, sedentary lifestyle, etc. The frequency of HTG-AP ranges from 5 to 15% [8,9]. According to the established etiology, HTG-AP disease is characterized by a tendency to a recurrent course and is often associated with polymorbidity.

Recent analytical reviews and meta-analyses have established significantly increased odds ratios for the development of persistent organ failure and mortality in patients with HTG-ANP [10,11].

The probability of AP recurrence in patients with lipemia is 7 times higher than in patients with AP without lipemia ( $p=0.02$ ). Patients with AP and lipemia are also 6 times more likely to have DM than patients without lipemia ( $p=0.02$ ) [12].

International recommendations on the use of afferent methods of treatment for various diseases and pathological conditions (2023) recommend the use of plasmapheresis in the treatment of HTG-AP [13]. Separate publications also testify to the expediency of using plasmapheresis in the treatment of HTG-AP [14].

## Objective

To evaluate the efficacy of plasmapheresis in the treatment of patients with hypertriglyceride-induced acute necrotic pancreatitis with priority early use of mini-invasive and delayed open surgical interventions, and to identify additional risk factors for an adverse course of the disease that led to laparotomy.

## Materials and Methods

The prospective observational cohort study included 82 patients with HTG-ANP who were treated from 2019 to 2025 at *Ivano-Frankivsk Regional Clinical Hospital*.

This work is part of the comprehensive scientific theme of the department of surgery and cardiac surgery of Ivano-Frankivsk National Medical University *Improving surgical tactics in diseases of the neuroendocrine system in order to improve treatment outcomes and improve the quality of life of patients* initiated in 2022 with a completion date of 2027 (State registration number: 0122U001740).

Study design: “case/main group of patients – control/patients of the comparison group”. The correlation between patient groups for assessing the effectiveness of plasmapheresis was studied based on the levels of total protein (TP), total cholesterol, triglycerides (TG), VLDL, low-density lipoproteins (LDL), high-density lipoproteins (HDL) in blood plasma, and atherogenic coefficient (AC). With the objective to identify additional prognostic risk factors for open surgery, correlations were examined for the presence of hypertension, DM, TG, and overweight, defined as a body mass index (BMI) greater than 25 kg/m<sup>2</sup>.

The main group comprised 53 out of 82 patients (65%), including 36 men (68%) and 17 women (32%), with a median age of 43 years [Q1–Q3=32–53]. In addition to intensive treatment and early-stage minimally invasive and open surgical interventions, plasmapheresis was administered to patients in the main group with HTG-ANP. The control group included 29 out of 82 (35%) patients, including 19 men (66%) and 10 women (34%) with a median age of 40 [Q1–Q3=38–47]. Plasmapheresis was not used in the patients of the control group. All patients included in the study had an alcoholic aetiology of the disease.

The study used the AP classification (Atlanta 2012 Classification) with the additions of the working group of experts. The criteria defined by the AP treatment guideline (China, 2021) and the recommendations of the American College of Gastroenterology (USA, 2024) were used in order to establish the diagnosis [3,4].

To establish the diagnosis of HTG-ANP GTG in the first hours after hospitalization, the level of TG in the blood plasma was determined, which was more than 2.21 (mmol/l), with a maximum of 3.79 (mmol/l) in the patients examined. In addition, TP, total cholesterol, TG, VLDL, LDL, HDL, AC, arterial hypertension, DM, and BMI levels were also measured.

According to the Atlanta 2023 Classification, with modifications from the expert working group, focal pancreonecrosis was identified in 34 out of 53 patients (64%) in the main group, and total or subtotal pancreonecrosis in 19 out of 53 patients (36%). Aseptic pancreonecrosis was confirmed in 26 patients (49%), while infected pancreonecrosis was observed in 27 patients (51%). In the control group, 19 out of 29 (66%) had focal pancreonecrosis, 10 out of 29 (34%) patients had total-subtotal pancreonecrosis; 8 out of 29 (28%) had aseptic pancreonecrosis, and 21 out of 29 (72%) patients had infected pancreonecrosis.

The most common comorbidities observed in patients from both groups were as follows: grade II–III hypertension – 44% (36/82), excessive body weight – 41% (34/82), systemic manifestations of atherosclerosis – 37% (30/82), DM – 23% (19/82), ischemic heart disease or previous myocardial infarction – 18% (15/82), varicose veins of the lower extremities and chronic venous insufficiency – 18% (15/82) of patients. 80 out of 82 patients (98%) had concomitant diseases. 40% (33/82) of patients had one concomitant disease each. Polymorbidity was established in 63% (52/82), 2 diseases were diagnosed in 37% (30/82), and 3 diseases in 27% (22/82) of the patients.

The basis of modern surgical tactics is a step-up approach, which involves the gradual use of invasive methods. The initial stage is laparoscopic, percutaneous or endoscopic drainage of fluid accumulations, which allows to reduce the infectious load and stabilize the patients' condition. In some patients, this stage was sufficient and allowed to avoid more aggressive interventions. In cases of ineffective drainage, minimally invasive methods of necrosequesrectomy were used, including endoscopic transluminal interventions and video-assisted retroperitoneal operations. They allowed to more radically remove areas of necrosis while maintaining a relatively low level of surgical trauma. Laparotomy was performed for limited indications in complex cases [15].

The first plasmapheresis session was started no later than one day after the patient's hospitalization in the presence of relevant criteria characteristic of AP and laboratory-confirmed plasma TG level of more than 2 (mmol/L), which is necessary for the diagnosis of HTG-AP.

Depending on the severity of the disease, plasmapheresis included 2–3 cycles of blood exfusion with the removal of 300 to 1500 ml of plasma and with the return of the patient's own erythrocyte mass to the bloodstream under the control of the level of TP in the blood plasma. The volume of plasmapheresis was 30–50% of the circulating plasma. The ratio of exfusion volumes was: blood components – 50%, protein-containing preparations – 25% and saline solutions – 25%. Plasmapheresis sessions were performed on a *DigiPla 90* device (China).

All procedures performed in the patient study met ethical standards for clinical practice and the 1964 Declaration of Helsinki, as amended.



Baseline demographic and clinical characteristics did not differ significantly between the groups ( $p>0.05$ ), thereby indicating satisfactory comparability of the study groups. Groups differed significantly in the rate of infected pancreatic necrosis (51% vs. 72%,  $p=0.012$ ), which was taken into account during the subsequent analyses.

Statistical analysis of the results was performed by using *MS Excel 2013* and the *IBM SPSS Statistics 26.0* software package. The obtained data were checked for the type of their distribution by the Lilliefors method and the W Shapiro-Wilk test. Since most of the data had a distribution different from normal, the median with interquartile range (Me [Q1; Q3]) was used as a measure of central tendency. Statistical analysis of categorical data was carried out by calculating the frequency of signs per 100 respondents. The reliability of the differences in the results obtained in different observation groups was assessed, and the null hypothesis was tested by calculating the chi-square ( $\chi^2$ ) goodness-of-fit criterion. Non-parametric criteria (Mann-Whitney, Wilcoxon) were used to test statistical hypotheses. The probability of an unmistakable prognosis of 95% ( $p=0.05$ ) was taken as a critical level of statistical significance. ROC analysis was used to identify potential prognostic risk factors for open surgery.

## Results

Minimally invasive surgical interventions were used in 90% (74/82) of the subjects, of whom, 91% (48/53) in the main group and 90% (26/29) in the control group.

In the main group, laparoscopic interventions for enzymatic peritonitis were performed in 85% (41/48) of the cases, laparoscopic interventions combined with percutaneous puncture and drainage interventions under ultrasound guidance for acute fluid accumulation in the omental bursa or retroperitoneal space in 75% (36/48) of the patients, and only puncture and drainage procedures under ultrasound guidance in 15% (7/48) of the patients. Minimally invasive procedures became the definitive method of surgical treatment in 60% (29/48) of the patients, including 3 out of 19 patients with total pancreonecrosis, in whom, it was possible to maintain the aseptic nature of the disease.

Laparoscopic interventions were performed in 92% (24/26) of the patients of the control group. In combination with percutaneous interventions under ultrasound guidance, laparoscopic interventions were used in 65% (17/26) of the cases, while percutaneous interventions alone were used in 31% (8/26) of the patients. Minimally invasive procedures became the definitive method of surgical treatment in 46% (12/26) of the patients in the control group.

The use of plasmapheresis in the early stages of HTG-ANP contributed to the ultimate effectiveness of minimally invasive interventions and a favorable course of the disease in 60% (29/48) of the patients in the main group, and in 46% (12/26) of the patients in the control group ( $p=0.238$ ).

The numerical values of the analyzed lipid metabolism indicators in the main group and the comparison group in the first days of the disease significantly exceeded the reference norm. Specifically, these included total cholesterol, TG, LDL, VLDL, HDL, and AC.

After plasmapheresis in the main group, the average level of total cholesterol decreased statistically significantly from 7.19 [6.99; 7.34] (mmol/L) to 5.26 [4.92; 5.53] (mmol/L) ( $p=0.001$ ). In the control group, the decrease in the mean value of this indicator was unreliable ( $p=0.122$ ), it was 7.54 [6.99; 8.01] (mmol/L) and decreased only to 6.97 [6.22; 7.84] (mmol/L).

Among the patients in the main group, the average TG level before treatment was 3.79 [3.51; 3.95] (mmol/L), whereas, after plasmapheresis, it was 2.21 [2.01; 2.52] mmol/L ( $p=0.002$ ). In the control group, changes in the average TG level were insignificant ( $p=0.067$ ) with medians of 3.68 [2.89; 4.05] (mmol/L) and 3.11 [2.76; 3.77] (mmol/L).

The average LDL level in the patients in the main group before treatment was 3.85 [3.62; 4.11] (mmol/L), while, after plasmapheresis, this indicator was significantly lower and amounted to 2.46 [2.19; 2.83] (mmol/L) ( $p=0.012$ ). In the control group, the median LDL was 3.74 [3.02; 4.11]

(mmol/L) before treatment and 3.11 [2.76; 3.79] (mmol/L) after treatment, respectively, with no statistically significant difference ( $p=0.072$ ).

No statistically significant difference between the mean VLDL and HDL levels before and after treatment was found in either the main group or the control group. Thus, the median VLDL values in the main group of the patients were 1.53 [1.21; 2.09] (mmol/L) and 1.45 [1.24; 2.22] (mmol/L) before and after treatment, respectively ( $p=0.132$ ). In the control group, the results were not significantly different, notably, 1.51 [1.25; 1.99] (mmol/L) before treatment and 1.44 [1.29; 1.87] (mmol/L) after treatment ( $p=0.121$ ). The average HDL level in the patients in the main group before treatment was 1.24 [0.89; 1.65] (mmol/L), and, after plasmapheresis, it was 1.23 [1.01; 1.59] (mmol/L), which was not statistically significant ( $p=0.354$ ). In the control group, the baseline level of this indicator was 1.27 [0.88; 1.73] (mmol/L), whereas, after treatment, it was 1.23 [0.94; 1.63] (mmol/L) ( $p=0.242$ ).

Plasmapheresis in the main group of patients led to a statistically significant decrease in the mean AC value. Thus, before treatment, the median value of this indicator was 4.80 [4.46; 4.97] (mmol/L), and, after plasmapheresis, it was 3.28 [3.02; 3.41] (mmol/L) ( $p=0.001$ ). In the control group, the mean AC values were 4.94 [4.35; 5.21] and 4.67 [4.29; 4.88] (mmol/L), before and after treatment, respectively, and no statistically significant difference was found ( $p=0.321$ ).

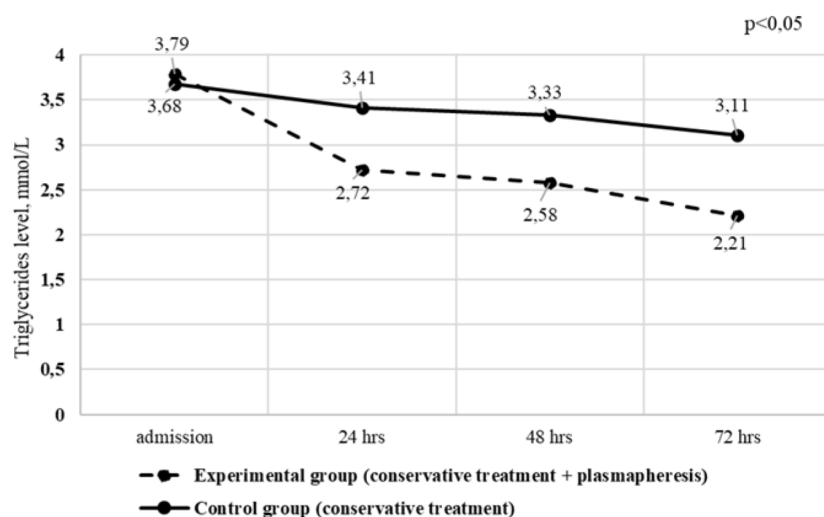
The level of TG in the main group of patients decreased by 28% compared to the initial values ( $p=0.003$ ) already after the first session of plasmapheresis (Fig. 1).

In the control group, the TG level decreased by only 7% over the same period of time ( $p=0.085$ ). While TG levels in patients in the main and control groups were approximately the same at the time of hospitalization, the difference in this indicator was statistically significant ( $p=0.021$ ) from the second to the fourth day.

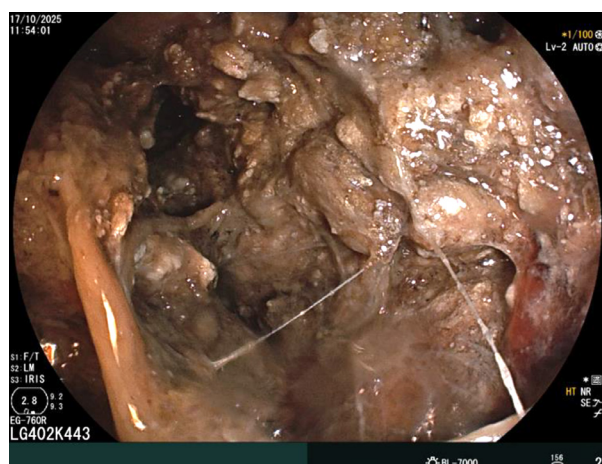
The timely use of plasmapheresis in HTG-ANP patients contributed to a significant decrease in the total cholesterol ( $p=0.001$ ), TG ( $p=0.002$ ), LDL ( $p=0.012$ ), and AC ( $p=0.001$ ). In the control group, the decrease in the average values of these indicators was unreliable.

In HTG-ANP, the course of the disease may be complicated by the development of localized fluid formations and PNPC, which we diagnosed mainly from the 4<sup>th</sup> week of the onset of the disease.

With PNPC, endoscopic transmural drainage was performed through the wall of the stomach or duodenum. Subsequently, a stable fistula was created between the stomach wall, less often the duodenum, and the PNPC wall. A stepwise pneumatic dilatation of the cystodigestive fistula to 15–18 mm was performed, which created conditions for the introduction of the working part of the gastroscope into the lumen of the PNPC. Subsequently, simultaneous or staged pancreatosequestrectomy was performed by using an endoscopic loop or Dormia basket. Finally, two 10 Fr 'pig-tail' endoprotheses and cystogastric drainage were installed in the PNPC lumen (Fig. 2).



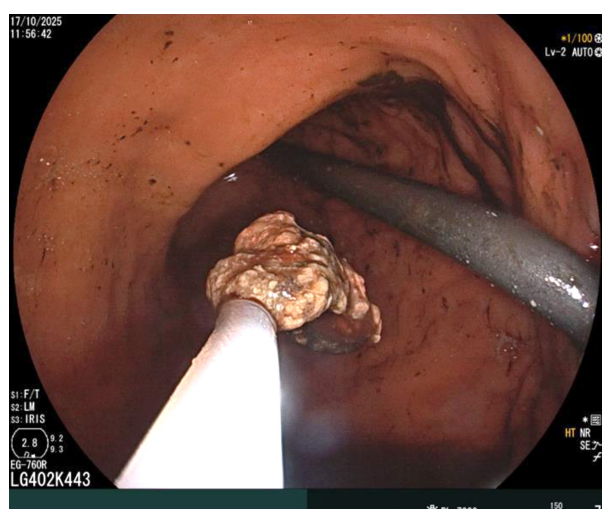
**Fig. 1.** Reduction of triglycerides in patients of the main and control groups



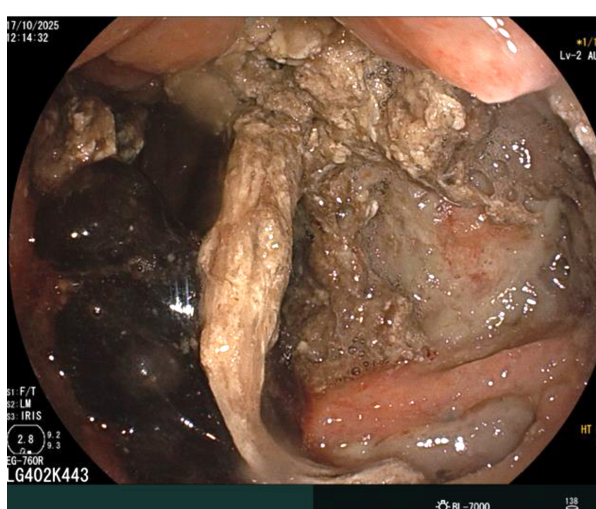
**Fig. 2.1.** Endophoto. Organized focus of pancreatic necrosis



**Fig. 2.2.** Endophoto. Enoscopic pancreatico-sequestrectomy using an endoscopic loop



**Fig. 2.3.** Endophoto. Removal of pancreatic sequestrum into the gastric lumen through the cystodigestive fistula



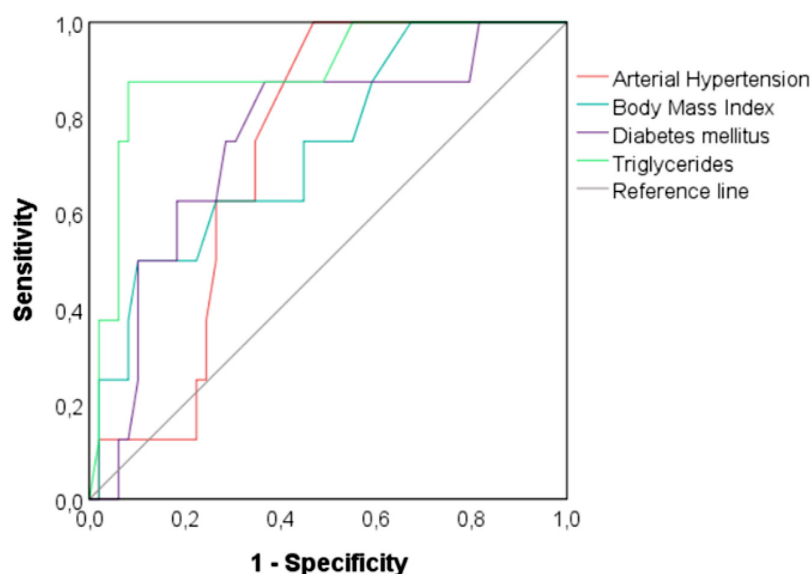
**Fig. 2.4.** Endophoto. Appearance of the pancreas after completion of staged endoscopic pancreatico-sequestrectomy

In case of a pancreatic duct defect, patients with PNPC underwent endoscopic retrograde cholangiopancreatography. When visualizing a defect in the pancreatic duct on a pancreatogram, a temporary pancreatic stent with a diameter of 5–7 Fr was placed so that its end was distal to the defect. Pancreatic stents were replaced every 2–3 months throughout the year to restore the integrity of the duct. Transmural stents were placed for 6–8 weeks to form a stable cystodigestive fistula.

In the main group with isolated fluid formations in the retroperitoneal space, isolated lumbarotomy was performed in 27% (13/48) of the patients. Endoscopic transmural interventions were performed in 23% (11/48) of the patients in the main group. In the control group, isolated lumbarotomy was performed in 54% (14/26) of the patients, and endoscopic transmural interventions were performed in 31% (8/26) of the patients.

ROC analysis was used to identify additional risk factors for the need for open surgery/laparotomy, both in the main group and in the control group. It was found that, for patients with HTG-ANP in both groups, additional prognostic risk factors for open surgery included arterial hypertension ( $p=0.042$ ), an excessive body weight with a BMI greater than 25 kg/m<sup>2</sup> ( $p=0.030$ ), DM ( $p=0.021$ ), and HTG ( $p=0.001$ ) (Fig. 3).





**Fig. 3.** ROC curves to predict open surgery in the core group

In the main group, when predicting open surgery, the area under the ROC curve was 0.73 (SI 95%: 0.60–0.86); for systolic blood pressure – 0.74 (SI 95%: 0.56–0.92); for BMI – 0.76 (SI 95%: 0.58–0.93); for blood glucose – 0.90 (SI 95%: 0.77–0.99); for TG – 0.90 (SI 95%: 0.77–0.99). The cut-off point at which a high probability of laparotomy can be predicted was 168 mmHg for systolic blood pressure; for BMI, this value was 27.6 (kg/m<sup>2</sup>); for blood glucose level, – 11.2 (mmol/L), and for blood plasma TG level, – 6.8 (mmol/L) – as shown in Table 1.

**Table 1.** Accuracy of indicators in predicting open surgery in the main group

|                                | Cut-off | AUC (CI 95%)     | Se, % | Sp, % | <i>p</i> |
|--------------------------------|---------|------------------|-------|-------|----------|
| Systolic blood pressure, mm Hg | ≥168    | 0.73 (0.60-0.86) | 75.00 | 65.30 | 0.04     |
| Body max index ≥ 25            | ≥27.6   | 0.74 (0.56-0.92) | 75.00 | 56.00 | 0.03     |
| Glucose level, mmol/l          | ≥11.2   | 0.76 (0.58-0.93) | 75.00 | 71.40 | 0.02     |
| Triglycerides mmol/l           | ≥6.8    | 0.90 (0.77-0.99) | 87.50 | 85.70 | <0.01    |

In the control group, when predicting open surgery, the area under the ROC curve was 0.74 (95% CI: 0.51–0.98) for blood glucose levels; 0.88 (95% CI: 0.73–0.99) for systolic blood pressure; BMI – 0.89 (95% CI: 0.78–0.99), and for plasma TG level – 0.98 (95% CI: 0.94–0.99) – see Fig. 4.

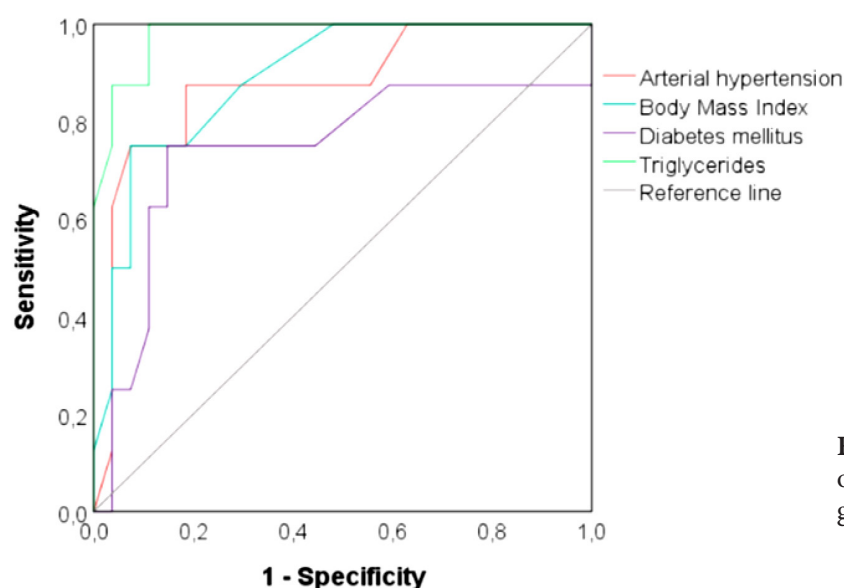
The threshold values for patients in the control group at the cut-off point for systolic blood pressure were 163 mmHg; for BMI – 28.2 (kg/m<sup>2</sup>); for blood glucose level – 11.4 (mmol/L), and for TG level in blood plasma – 7.1 (mmol/L) – see Table 2.

**Table 2.** Accuracy of indicators in predicting open surgery in the control group

|                                | Cut-off | AUC (CI 95%)     | Se, % | Sp, % | <i>p</i> |
|--------------------------------|---------|------------------|-------|-------|----------|
| Systolic blood pressure, mm Hg | ≥163    | 0.88 (0.73-0.99) | 87.50 | 81.50 | <0.01    |
| Body max index ≥ 25            | ≥28.2   | 0.89 (0.78-0.99) | 87.50 | 70.40 | <0.01    |
| Glucose level, mmol/l          | ≥11.4   | 0.74 (0.51-0.98) | 75.00 | 67.00 | 0.04     |
| Triglycerides mmol/l           | ≥7.1    | 0.98 (0.94-0.99) | 87.50 | 89.00 | <0.01    |

Therefore, in patients of both groups with HTG-ANP, such additional prognostic risk factors for open surgery were established as arterial hypertension ( $p=0.042$ ), an excessive body weight with a BMI greater than 27.6 kg/m<sup>2</sup> ( $p=0.030$ ), DM ( $p=0.021$ ), and HTG ( $p=0.001$ ).





**Fig. 4.** ROC curves to predict open surgery in the control group

Among the examined patients with acute necrotic pancreatitis, open surgical interventions were performed in 36% (27/74) of the operated patients, including 29% (14/48) in the main group and 50% (13/26) in the control group.

Such surgeries were performed when the possibilities of mini-invasive technologies or endoscopic interventions were practically exhausted. The indications for laparotomy mostly included infected subtotal and total pancreatic necrosis, pancreatic sequestration, purulent parapancreatitis, erosive bleeding, etc. Transverse laparotomy was considered the preferred surgical approach. One intervention was performed in 19 patients, and 2 interventions were needed in 4 patients.

Postoperative mortality in the main group of patients was 10.4% (5 out of 48 operated patients died). In the control group, the postoperative mortality was 15.3% (4 out of 26 operated patients died). The overall mortality in the main group was 9.43% (5/53), whereas, in the control group, it was 13.7% (4/29).

## Discussion

HTG is one of the signs of most types of hyperlipidemia, and it remains an important factor in the development of cardiovascular diseases, including coronary heart disease, Type II diabetes mellitus, obesity, etc. [6,7]. Acquired HTG is influenced by alcohol abuse, among other causes.

Acute pancreatitis occurring against the background of HTG is characterized by a tendency to a recurrent course and polymorbidity [1]. According to our data, in HTG-ANP, 98% (80/82) of the patients had concomitant diseases, and polymorbidity was established in 63% (52/82) of the patients. Alcohol abuse was the dominant cause of the disease in the examined patients.

International recommendations on the use of afferent methods of treatment for various diseases and pathological conditions (2023) recommend the use of plasmapheresis in the treatment of HTG-AP [13]. In patients with HTG-ANP, a timely diagnosis of the disease and early use of plasmapheresis made it possible to correct lipid metabolism disorders in the short term and achieve a reduction in the total cholesterol ( $p=0.001$ ), TG ( $p=0.002$ ), HDL ( $p=0.012$ ), and AC ( $p=0.001$ ) levels in the short term.

This also ensured the use of mini-invasive interventions as the final methods of surgical treatment in 60% (29/48) of the patients in the main group. In the control group, this indicator was 46% (12/26) of the patients ( $p=0.238$ ).

In patients with HTG-ANP, plasmapheresis should be used in the first days of the disease in order to normalize lipid metabolism. The significance and effectiveness of this method in the treatment of HTG-ANP, especially with the transition of the disease to the period of purulent-septic complications, are low. Of paramount importance are the screening of the pancreas by using radiation methods of examination, rational intensive care, antibacterial treatment, the diet and nature of nutrition, prevention of enteral insufficiency, secondary infection of the pancreas, etc. The implementation of these components made it possible to ensure a favorable course and aseptic nature of the disease, even with widespread pancreatic necrosis, including in 3 patients with total pancreatic necrosis.

In the development of local purulent-septic complications, it is of importance to use isolated lumbarotomy and endoscopic transmural interventions, which ensure the performance of pancreatosequestrectomy. An important condition for preventing PNPC recurrence is the restoration of the integrity of the pancreatic duct. Therefore, patients with PNPC and a detected pancreatic duct defect underwent endoscopic retrograde cholangiopancreatography with stenting. In some patients, endoscopic transmural interventions with pancreatosequestrectomy for PNPC and isolated lumbarotomy for retroperitoneal fluid collections contributed to an improvement of the disease course and allowed avoiding laparotomy.

Indications for open intervention were present in the examined patients who were infected with subtotal and total pancreatonecrosis, purulent parapancreatitis, and erosive bleeding, which generally corresponds to international guidelines [3,4].

In HTG-ANP patients, hypertension ( $p=0.042$ ), BMI more than  $27.6 \text{ kg/m}^2$  ( $p=0.030$ ), DM ( $p=0.021$ ), and HTG ( $p=0.001$ ) were established as additional prognostic risk factors for laparotomy, which was performed mainly for the development of purulent-septic complications that could not be eliminated by mini-invasive interventions.

## Conclusions

Timely diagnosis of hypertriglyceride-induced acute necrotic pancreatitis with an early use of plasmapheresis provided patients with a significant reduction in triglyceride levels ( $p=0.002$ ), low-density lipoproteins ( $p=0.012$ ), total cholesterol ( $p=0.001$ ), and the atherogenicity coefficient ( $p=0.001$ ). Plasmapheresis in the early stages of hypertriglyceride-induced acute necrotic pancreatitis had a positive effect on the course of the disease and ensured the final effectiveness of mini-invasive surgical interventions in 60% of the patients in the main group. In the control group, minimally invasive procedures became the definitive method of surgical treatment in 46% of the patients ( $p=0.238$ ). With the development of purulent-septic complications of pancreatic necrosis, the widespread use of plasmapheresis is inappropriate. In cases of local complications of pancreonecrosis in the form of PNPC, endoscopic transmural interventions with pancreatosequestrectomy contribute to improving the course and prognosis of the disease.

Additional prognostic factors for complicated hypertriglyceride-induced acute necrotic pancreatitis, accompanied by purulent-septic complications and requiring laparotomy, are arterial hypertension, a body mass index greater than  $27.6 \text{ (kg/m}^2\text{)}$ , diabetes mellitus, and hypertriglyceridemia.

## Author contributions:

**I. S.:** conceptualization, data curation, project administration.

**R. K.:** project administration, supervision, writing – review and editing.

**V. P.:** methodology, validation.

**I. H.:** formal analysis, investigation.

**S. G.:** formal analysis, investigation.

**S. S.:** software.

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