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ТРОМБОЗ ВОРОТНОЙ ВЕНЫ ПРИ ЦИРРОЗЕ ПЕЧЕНИ. ЧАСТЬ 2: ЛЕЧЕНИЕ, ПЕРВИЧНАЯ И ВТОРИЧНАЯ ПРОФИЛАКТИКА

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Portal Vein Thrombosis in Liver Cirrhosis. Part 2: Treatment, Primary and Secondary Prevention

Резюме

В большинстве случаев тромбоз воротной вены прогрессирует без лечения, спонтанная реканализация воротной вены развивается у 42 % больных циррозом печени. Существующие стратегии лечения включают назначение антикоагулянтов, проведение интервенционных мероприятий, таких как трансъюгулярное внутрипеченочное портосистемное шунтирование или эндоваскулярный фибринолиз. Антикоагулянтная терапия имеет определенные трудности у пациентов с циррозом печени из-за сложного профиля гемостаза, склонности как к геморрагиям, так и к гиперкоагуляции. Помимо традиционных антикоагулянтов (препараты гепарина, фондапаринукс, антагонисты витамина К) в последние годы при тромбозе воротной вены широко используются прямые оральные антикоагулянты. Ранее тромбоз воротной вены считался противопоказанием к выполнению трансъюгулярного внутрипеченочного портосистемного шунтирования, в настоящее время метод часто применяется с целью восстановление портального кровотока через шунт и предотвращения повторного тромбоза. Эндоваскулярный фибринолиз по-прежнему остается опцией специализированных центров для «сложных» больных. В случаях повышенного риска венозных тромбоэмболий пациентам с циррозом печени рекомендуется профилактика препаратами низкомолекулярного гепарина или прямыми оральными антикоагулянтами, однако дальнейшие исследования должны уточнить их эффективность в этом аспекте. В обзоре освещены данные об особенностях терапии, первичной и вторичной профилактики тромбоза воротной вены у больных циррозом печени. Несмотря на существующие клинические рекомендации по ведению больных цирротическим тромбозом воротной вены, выбор той или иной стратегии, прежде всего, зависит от индивидуализированной оценки рисков и преимуществ каждого из методов лечения.

Ключевые слова: *тромбоз воротной вены, цирроз печени, лечение, антикоагулянты, трансъюгулярное внутрипеченочное порто-системное шунтирование, профилактика*

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Abstract

In most cases, portal vein thrombosis progresses without treatment; spontaneous recanalization of portal vein develops in 42 % of patients with liver cirrhosis. Effective treatment strategies include administration of anticoagulants, interventional procedures such as transjugular intrahepatic porto-systemic shunt or endovascular fibrinolysis. Anticoagulant therapy has certain difficulties in patients with liver cirrhosis due to the complex profile of hemostasis, a tendency to both hemorrhages and hypercoagulation. In addition to traditional anticoagulants (heparin preparations, fondaparinux, vitamin K antagonists), direct oral anticoagulants have been widely used in recent years for portal vein thrombosis. Previously, portal vein thrombosis was considered a contraindication to performing transjugular intrahepatic porto-systemic shunt, currently the method is often used to restore portal blood flow through the shunt and prevent repeated thrombosis. Endovascular fibrinolysis is still an option for specialized centers for «difficult» patients. In cases of increased risk of venous thromboembolism, patients with liver cirrhosis are recommended to be prevented with low-molecular-weight heparin or direct oral anticoagulants, but further studies should clarify their effectiveness in this aspect. The review highlights data on the features of therapy, primary and secondary prevention of portal vein thrombosis in patients with liver cirrhosis. Despite the existing clinical recommendations for management of patients with cirrhotic portal vein thrombosis, the choice of a particular strategy primarily depends on an individualized assessment of risks and benefits of each treatment method.

Key words: *portal vein thrombosis, liver cirrhosis, treatment, anticoagulants, transjugular intrahepatic porto-systemic shunt, prevention*

Conflict of interests

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APPT — activated partial thromboplastin time; CI — confidence interval; INR — international normalised ratio; LMH — low molecular heparin; UFH — unfractionated heparin; HR — hazards ratio; OR — odds ratio; PVT — portal vein thrombosis; TIPSS — transjugular intrahepatic porto-systemic shunt

Treatment

The natural course of portal vein thrombosis (PVT) in hepatic cirrhosis is variable; this heterogeneity makes PVT a unique condition among venous thromboses [1]. Spontaneous portal vein repatency is observed in 42 % of PVT cases [2-4]. Its incidence reaches 70 % in compensated cirrhosis or partial thrombosis [4], whereas in decompensated cirrhosis or in patients on the liver transplantation list, spontaneous repatency is significantly less frequent [5]. Predictors of spontaneous improvements in portal vein thrombosis are unknown.

In asymptomatic patients, who are not candidates for liver transplant and have thrombosis in their small intrahepatic branches of the portal vein or minimal occlusion (< 50 % of the vein lumen), follow-up is usually enough [6, 7].

At the same time, in 33–70 % of patients with hepatic cirrhosis, when left untreated, portal vein thrombosis progresses [3, 8]. According to clinical guidelines, a decision to initiate therapy is based on the extent of the thrombus, presence of symptoms, and need for a liver transplant [6, 7, 9, 10]. If bowel ischaemia is suspected, early anticoagulant therapy is initiated; it is also recommended to consult a surgeon and a specialist in intensive care and interventional radiology [7].

PVT development in cirrhosis impacts the possibility and outcomes of liver transplantation. Candidates for a transplant need to have at least a partially re-canalised portal vein to ensure portal blood flow to the transplant using end-to-end anastomosis, which reduces post-surgery morbidity and mortality. If the vein is not re-canalised, the purpose of PVT management is to prevent thrombus growing, especially to prevent mesenteric vein involvement [6, 7].

Therapy is also recommended in patients with chronic occlusive PVT or cavernous portal vein transformation to prevent repeated thrombosis and, to a lesser extent, to ensure vein re-patency, especially in hereditary thrombophilia, progressive thrombosis, bowel ischaemia caused by thrombotic involvement of the mesenteric vein, or in patients waiting for liver transplantation [10].

Possible therapies of the portal vein thrombosis in cirrhosis patients include anticoagulants, transjugular intrahepatic porto-systemic shunt, endovascular clot lysis.

PVT is associated with a high risk of varicose bleeding, that is why before initiation of anticoagulants, patients with cirrhosis should undergo endoscopic vein ligation and use β-adrenoreceptor blocking agents [9]. However, anticoagulation therapy should not be delayed until complete esophagus vein eradication and b-adrenoreceptor blocking [7].

Anticoagulants

Data from retrospective studies [2, 11-15] and some meta-analyses [3, 16-18] show that, in cirrhosis patients, anticoagulants are an efficient and safety therapy of portal vein thrombosis. They promote any degree of vein re-patency in 66.6–71.5 % of cases; complete re-patency

was observed in 40.8–53 % of patients; and the rate of thrombosis progression, despite the therapy, did not exceed 5.7–9 % [3, 16-18]. Anticoagulation therapy in PVT patients with liver cirrhosis was associated with a higher rate of vein re-patency (44.4 % vs. 20.0 %, P = 0.016) and with lower thrombosis progression rates (7.4 % vs. 30.0 %, P = 0.026) vs. no therapy[19]. According to a meta-analysis, unlike observation, anticoagulants showed a 4-fold increase in the probability of portal vein re-patency (odds ratio (OR) 4.44; 95 % confidence interval (CI) 3.11–6.32) and 3-fold reduction in the probability of cirrhotic PTV progression (OR 0.33; 95 % CI 0.18–0.62) [20].

Nevertheless, the rate of portal vein re-patency after coagulation therapy for PVT in cirrhotic patients is lower than in other venous thromboses [1]. According to E.G. Driever et al., it is associated with the fact that cirrhotic PVT manifested as thickening of the portal vein wall intima, similar to intima fibrosis, and a fibrin-rich blood clot was observed only in one third of cases. The authors believe that the lack or small amounts of fibrin is a cause of relatively low rates of portal vein re-patency in cirrhosis [21].

According to meta-analyses, anticoagulation therapy has a positive effect on the course and mortality rates in cirrhotic patients by reducing the risk of esophagus bleeding [3, 16] and improving overall survival rates [18, 22], which to some extent depend on successful portal vein re-patency.

Anticoagulation therapy is safe and has a comparable rate of haemorrhages as compared to the patients who did not have any therapy [3, 18, 23, 24]. A history of varicose bleeding, platelet count below $50x10^9$/L and low serum albumin are the key risk factors of bleeding in patients receiving anticoagulation therapy [25, 26]. Complications of severe cirrhosis were observed in cases where no portal vein re-patency was achieved [25]. A retrospective study demonstrated that anticoagulation therapy of PVT did not increase the rate of bleeding in cirrhotic patients (14.8 % vs. 24 %, P = 0.343), including major bleedings (3.7 % vs. 6 %, P = 0.665) and varicose haemorrhages (3.7 % vs. 16 %, P = 0.109) [19], as compared to no therapy. A meta-analysis showed that anticoagulants did not cause any increase in the risk of bleeding (OR 1.21; 95 % CI 0.75–1.97), including major bleedings (OR 0.98; 95 % CI 0.49–1.95) and varicose haemorrhages (OR 0.35; 95 % CI 0.12–1.01) [20].

The modern anticoagulation therapies include heparin preparations, fondaparinux, vitamin K antagonists and direct oral anticoagulants.

Heparins

First, heparin therapy includes injections of unfractionated and low molecular heparins. Once bound to antithrombin III, unfractionated heparin (UFH) neutralises factor Xa and thrombin. Heparin therapy requires activated partial thromboplastin time (APPT) monitoring: the therapeutic margin should be 1.5–2 times higher than the normal APPT value. Due to these limitations and possible complications (heparin-induced low platelet count, osteoporosis, etc.), UFH is currently less common than low molecular heparin (LMH). UFH can be prescribed in renal insufficiency and/or in suspected bowel ischaemia, as it can be easily discontinued; however, intravenous administration makes it impossible to use the preparation for a long time [10].

LMH neutralises mainly factor Xa. It is administered subcutaneously once or twice daily in a fixed dose for prevention or depending on the body weight — for therapeutic use. It does not require laboratory monitoring; still, laboratory tests are recommended in obese patients, patients with renal failure (glomerular filtration rate of less than 15 mL/min) and in pregnant women [27].

Due to the need of parenteral administration, low molecular heparin reduces compliance and patient's quality of life, that is why it is used as initiation therapy and then patients switch to vitamin K antagonists or direct oral anticoagulants. However, with refractory abdominal dropsy, where periodic paracentesis is required, or because of challenges with long-term monitoring of the international normalised ratio (INR), LMH is more preferable than oral anticoagulants [27].

LMH is the most acceptable variant in any Child-Pugh liver cirrhosis, while unfractioned heparin can be a frontline therapy in acute kidney injury until their function normalises [28].

The major concerns about the use of LMH are associated with its efficacy and safety in cirrhotic patients, similar to patients without liver damage, given this cohort has lower antithrombin III activity. *In vitro* and *in vivo* studies showed that LMH is efficient and safe for patients with PVT and liver cirrhosis, despite lower levels of anti-Xa and antithrombin III [23, 24, 26, 29]. For instance, dalteparin and enoxaparin resulted in portal vein re-patency in 66.1 % and 78.5 % of PVT cases, respectively [29, 30]. The rate of complete or partial portal vein re-patency after nadroparin/warfarin therapy was higher vs. controls, both for cirrhotic PVT with acute varicose bleeding (67.4 % vs. 39.5 %, P = 0.009) [23] and without bleeding (62.5 % vs. 34.4 %, P = 0.024) [24]. In addition to anticoagulants (OR 4.189; 95 % CI 1.660–10.568; P = 0.002) predictors of therapy efficiency were low Child-Pugh scores (OR 0.692; 95 % CI 0.488–0.982; P = 0.039) and D-dimer values below 2.00 μg/mL (OR 3.600; 95 % CI 1.134–11.430; P = 0.030) [23, 24]. LMH (enoxaparin or dalteparin) facilitated portal vein re-patency in 61.5 % of patients with liver cirrhosis and PVT, the probability of which increased with a favourable Child-Pugh category and short duration of thrombosis [26].

Lower doses of LMH did not reduce its efficiency [31]. For instance, enoxaparin 1 mg/kg twice daily demonstrated similar results, but was associated with fewer complications (4-fold reduction in the risk of non-varicose bleeding) vs. 1.5 mg/kg daily [30]. At the same time,

it is assumed that the efficacy of a fixed dose of dalteparin is 2.6 times lower than when the preparation dose is based on the body weight [29].

Fondaparinux

Fondaparinux inhibits factor Xa by selectively binding to antithrombin III. Unlike heparin, it does not inhibit thrombin or platelet factor IV, which reduces the risk of heparin-induced low platelet count [32]. A fixed dose of the preparation is administered once daily without laboratory monitoring, so it is more convenient than LMH.

In a retrospective study of fondaparinux vs. LMH, fondaparinux demonstrated a higher probability of PVT elimination in patients with liver cirrhosis (77 % and 51 %; P = 0.001); however, it was associated with a higher number of bleedings (27 % and 13 %; P = 0.06) [33]. It is suggested that fondaparinux can be an agent of choice in cirrhotic patients with extremely low platelet count.

Vitamin K antagonists

Vitamin K antagonists impair carboxylation and reduce the activity of vitamin K-dependent blood clotting factors. Due to a narrow therapeutic window and drug-drug interactions, their administration required INR monitoring. The therapeutic range corresponds to INR 2.0–3.0 (target INR: 2.5) [9].

Determination of the therapeutic range of vitamin K antagonists in cirrhotic patients is challenging because of the initially longer prothrombin time. That is why the therapeutic range requires lower doses, therefore, patients can receive a low dose. On the other hand, because of higher values the normal INR is not suitable for cirrhotic patients, that is why a modified INR (liver INR) can be used as an alternative [9].

Vitamin K antagonists are recommended in cirrhotic patients with Child-Pugh class A; still, they should be used with caution, since initially modified INR can affect its target values [28].

Vitamin K antagonists used as maintenance therapy are efficient and safe [13], and their rates of re-patency and side effects are similar to those of LMH [2, 23, 24]. Unlike untreated patients, patients receiving warfarin had higher rates of portal vein re-patency (P = 0.011); thrombosis improved in 68.2 % and 25 % of cases, remained stable in 18.2 % and 37.5 % of cases, and progressed in 13.6 % and 37.5 % of cases, respectively [2]. In a randomised study, the rate of portal vein re-patency was twice as high with warfarin vs. controls (71.9 % vs. 34.4 %, P = 0.004); anticoagulation therapy was a predictor of re-patency (OR 2.776; 95 % CI 1.307–5.893; P = 0.008) and was not associated with a higher risk of bleeding [34].

Direct oral anticoagulants

Direct oral anticoagulants directly inhibit thrombin (dabigatran) or factor Xa (rivaroxaban, edoxaban, betrixaban and apixaban) without antithrombin III involvement or impaired carboxylation of vitamin K-dependent blood clotting factors. In addition to fixed oral doses, their advantages include no need for laboratory monitoring and no impact on INR values [9].

Given a possible-drug-drug interaction, the concentration or efficacy of direct oral anticoagulants can be impacted by P-glucoprotein preparations, as well as medications modifying CYP3A4 activity [35].

Pharmacokinetics of direct oral anticoagulants in liver cirrhosis has been understudied. *In vitro* and *in vivo* studies show that the efficacy of preparations inhibiting factor Xa can be lower in cirrhotic patients; it is a result of impairments at various stages of drug metabolism (binding to plasma proteins, cytochrome p450 function, bile excretion and renal clearance) [36, 37].

Direct oral anticoagulants can be safely used in patients with Child-Pugh class A. In Child-Pugh class B or where creatinine clearance is below 30 mL/min, they should be used with caution because of possible accumulation, which requires dose reduction [28, 35], while rivaroxaban is contraindicated in class B cirrhosis patients [38]. Direct oral anticoagulants are not recommended in Child-Pugh class C or with creatinine clearance below 15 mL/min [28, 35].

Direct oral anticoagulants are safe and efficient in thromboembolic conditions in liver cirrhosis [39], including portal vein thrombosis. Edoxaban was more efficient in complete PVT elimination in cirrhosis patients vs. warfarin (70 % and 20 %), while thrombosis progression was less common (5 % and 47 %, respectively) [40]. Rivaroxaban was superior to warfarin in the rate of portal vein re-patency and was more efficient in thrombosis relapses [41]. In a prospective study by M.-H. Ai et al. of 6-month rivaroxaban or dabigatran therapy of chronic PVT in cirrhosis patients, a higher rate of complete/partial portal vein re-patency and better blood flow were observed vs. controls (P < 0.05), while the risk of haemorrhage was similar (P > 0.05) [42]. In non-cirrhotic PVT, direct oral anticoagulants were more efficient than vitamin K antagonists (OR 4.33; 95 % CI 2.4–7.83), while in cirrhotic thrombosis — more efficient than no therapy (OR 3.86; 95 % CI 1.49–10.03) or vitamin K antagonists (OR 30.99; 95 % CI 7.39–129.87) [20, 43]. According to a meta-analysis, direct oral anticoagulants and vitamin K antagonists were effective in PVT re-patency in 87.3 % and 44.1 % of cirrhotic patients with PVT; at the same time, direct oral anticoagulants were associated with a higher rate of vein re-patency (OR 1.67; 95 % CI 1.02–2.74) and a lower risk of thrombosis progression (OR 0.14; 95 % CI 0.03–0.57) [44].

The rate of bleeding when taking direct oral anticoagulants was similar or lower than with the use of traditional anticoagulants [20, 40, 41]. In retrospective studies [39, 45-47] and meta-analyses [20, 44, 48, 49], direct oral anticoagulants in liver cirrhosis had safety profiles similar to those of traditional anticoagulants; however,

the risk of bleeding was higher in progressive disease [46]. In cirrhotic PVT, direct oral anticoagulants were associated with a lower total risk of a major bleeding (OR 0.29; 95 % CI 0.08–1.01) vs. vitamin K antagonists, but they had a similar total risk of varicose bleeding (OR 1.29; 95 % CI 0.64–2.59) and death (OR 0.31; 95 % CI 0.01–9.578) [44].

Duration and predictors of successful therapy

The highest probability of the efficient anticoagulation therapy is observed if the period between PVT diagnosis and therapy initiation is less than six months [8, 31]; however, according to other data, early anticoagulation (within 1–2 weeks) is also associated with higher rates of portal vein re-patency [25]. Therefore, the optimal timing for anticoagulation therapy initiation is still unclear [37].

The mean time for portal vein re-patency is 5.5–8 months [8, 50]; however, there are reports on delayed response one year after therapy [50]. The therapy lasts at least half a year, and patients with superior mesenteric vein thrombosis and bowel ischaemia should be on life-long anticoagulation therapy [6, 9].

Other factors of good response to therapy are a mild hepatic disease, mild thrombosis, superior mesenteric vein thrombosis of less than 50 %, no history of bleeding associated with portal hypertension, and smaller spleen [13, 18, 51].

Therapy efficiency should be evaluated every 2–3 months with imaging [27].

Once therapy was discontinued after portal vein repotency, thrombosis relapses were observed in 27–56.6 % of cases 2–5 months later (median time to relapse: 4 months) [25, 26, 29]. The risk of thrombosis relapse after dalteparin therapy increased 3.1–3.9-fold if therapy was initiated 3–6 months after diagnosis [29]. According to the recommendations on thrombosis relapse prevention, therapy should continue for several more months after vein re-patency or until liver transplantation [9].

Transjugular intrahepatic porto-systemic shunt (TIPSS)

Earlier portal vein thrombosis was a contraindication to TIPSS. Current guidelines list the following indications for TIPSS in patients with hepatic cirrhosis and PVT: inadequate response or contraindications to anticoagulants; chronic PVT/portal cavernoma with severe sequelae of portal hypertension (recurring varicose bleeding or abdominal dropsy), refractory to drug therapy; chronic PVT preventing physiological anastomosis between the transplant and recipient's portal vein [6, 7, 10, 52]. Liver transplant candidates with progressive PVT with no response to anticoagulation therapy undergo TIPSS, which prevents thrombosis aggravation and complete portal vein occlusion [9].

The purpose of TIPSS is restoration of portal blood flow with the help of a shunt and prevention of thrombosis recurrence.

The most common indication for TIPSS in cirrhosis patients with PVT was not thrombosis itself, but therapy-resistant consequences of hypertension. Successful TIPSS was associated with clinical improvements of cirrhosis, low incidence of thrombosis recurrences and recurrent portal bleeding, reduced need for systemic anticoagulation, which was required only in prothrombotic condition [53, 54].

After TIPSS, re-patency rates varied from 70 to 100 % [53, 55, 56]. Meta-analyses showed that re-patency and complete re-patency after TIPSS was 81–84.4 % and 73–74.61 %, respectively; the probability of severe complications exceeds 10 % [55, 57, 58]. Unlike anticoagulants, TIPSS was more efficient in portal vein re-patency and prevention of bleeding relapses; it did not increase the risk of side effects, however, the survival rates did not improve as well [55, 59, 60]. If compared to the conservative therapy (endoscopic ligation of esophagus veins and propranolol), TIPSS was associated with better portal vein re-patency outcomes (95 % vs. 70 %; P = 0.03), thrombosis relapses (5 % vs. 33 %; P = 0.06), rate of recurrent varicose bleedings (15 % vs. 45 % one year later and 25 % vs. 50 % two years later, respectively; OR 0.28; 95 % CI 0.10–0.76; P = 0.008); however, patient survival rates were similar [61]. The group of successful TIPSS after chronic PVT had lower portal vein pressure (27.15 vs. 19.74 mm Hg, P < 0.001); mortality rates were comparable (12.9 % vs. 19.2 %; P > 0.05); while bleeding recurrences (14.7 % vs. 30.8 %; P = 0.017) were lower than in unsuccessful TIPSS procedures [56]. In patients with cirrhotic PVT with varicose bleeding, TIPSS more often resulted in complete portal vein re-patency (85.5 % vs. 19.6 %, P < 0.001) and lower rates of 5-year recurrent esophagus vein bleeding (31.0 % vs. 50.1 %; P = 0.017), than in endoscopic management and anticoagulants [62].

In patients with frequent PVT caused by hepatic cirrhosis, awaiting transplantation, TIPSS did not affect the rate of complications, outcomes, duration of transplantation or the need for blood preparations.

TIPSS is justified for PVT with cavernous transformation [63]; however, it is associated with lower technical success rates, which increase to 90 % (ranging from 75 % to 100 %) with the use of a modified transplant or transhepatic approach [64]. In this situation, portal vein re-patency is achieved with angioplasty/stenting and TIPSS insertion [65].

Technical complications with TIPSS emerge in advanced PVT because of the impossibility to puncture the intrahepatic branch of the portal vein, so the transcutaneous approach is used, which is more risky.

Unlike anticoagulants, endoscopic management or endovascular clot lysis, TIPSS can increase the risk of hepatic encephalopathy (rate: 25–32 %) [62, 66]; however, it was not confirmed in a number of studies [56, 61].

Endovascular clot lysis

Experience in using local or systemic clot lysis, also in combination with TIPSS or anticoagulants, in patients with cirrhosis-associated PVT is limited. In cirrhotic PVT, clot lysis usually results in partial portal vein repatency and is more efficient if combined with thrombectomy [53]. In PVT patients, clot lysis combined with anticoagulants had efficiency similar to anticoagulation therapy; however, it was associated with a higher risk of morbidity and mortality [67].

Similar to TIPPS, endovascular clot lysis improved PVT in cirrhotic patients (85 % and 70 %; P = 0.304); clot lysis was more often associated with dissolution of blood clots in superior mesenteric (P = 0.048) and splenic veins (P = 0.02) [66].

Current guidelines recommend that clot lysis in patients with persistent bowel ischaemia despite anticoagulants is performed in specialised clinics [7, 68].

Contraindications for clot lysis include recent stroke, GIT bleeding, recent orthopaedic, cerebral or spinal trauma and an intracranial tumour [53].

Primary PVT prevention in hepatic cirrhosis

Patients with hepatic cirrhosis and a high risk of venous thromboembolism are recommended to undergo prevention with LMH or direct oral anticoagulants with an acceptable safety profile, although their efficiency is unclear. For Child-Pugh class C cirrhosis, direct oral anticoagulants are not used for prevention of thrombotic complications [28].

This recommendation is based on a randomised study, which demonstrated that enoxaparin therapy in cirrhosis patients prevented PVT [69]. The enoxaparin group demonstrated lower rates of PVT (8.8 % vs. 27.7 %, P = 0.048) and hepatic decompensation (38.2 % vs. 83.0 %, P < 0.0001) vs. placebo; enoxaparin also reduced the risk of deaths without a higher risk of bleeding, which may be associated with a better barrier function of the bowel and reduced bacterial translocation [69].

Post-splenectomy initiation of antithrombin III concentrate or antithrombin III, danaparoid sodium and warfarin in patients with a high risk (antithrombin III activity of less than 70 % and splenic vein diameter of less than 10 mm) and a very high risk (splenic vein diameter of over 15 mm) of PVT resulted in reduction in the rate of thrombosis [70].

Unlike aspirin, warfarin was more efficient in prevention of PVT after laparoscopic splenectomy in cirrhosis patients (no thrombosis in 38.5 % and 12.8 % of cases, respectively, P = 0.010), and had a hepato- and nephroprotective effect [71].

Therapy of liver cirrhosis patients with direct oral anticoagulants had a good safety profile, absence of venous thrombosis and no high risk of bleeding, lower rates of ischaemic stroke in liver cirrhosis [48, 72-75].

At the same time, there is some evidence that thrombosis prevention with low molecular or unfractioned heparin did not reduce the risk of venous thromboembolism (OR 0.94; 95 % CI 0.23–3.71) in patients admitted with hepatic cirrhosis [76, 77] and mortality, but tended to increase the risk of bleeding when unfractioned heparin was used [76].

Secondary prevention of PVT after liver transplantation

Post-transplantation portal vein thrombosis, especially long-lasting, is a risk factor of recurrence in case of non-anatomical anastomosis [5]. In addition to presurgery thrombosis, risk factors of post-transplantation PVT include slow portal blood flow after reperfusion (< 1,300 mL/min or < 65 mL/min/100 g), partial thrombectomy, damaged vein intima during thrombectomy, inappropriate reconstruction of inflow to the portal vein, thrombophilic impairments in the recipient [27]. Patients with risk factors and without blood-clotting disorders, transplant dysfunction or low platelet count (< 30–50x10^9/L) within first 24 hours after surgery, have LMH therapy (1 mg/kg) for at least two months, if there are no complications, the therapy can then be prolonged based on individual considerations [78].

Conclusion

The article describes the therapy, possible measures for primary and secondary prevention of portal vein thrombosis in patients with liver cirrhosis. Despite the existing clinical recommendations for the management of cirrhosis patients with PVT, selection of a therapeutic strategy depends mostly on an individualised evaluation of risks and benefits of each therapy.

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Список литературы/ References:

1. Anton A., Campreciós G., Pérez-Campuzano V. et al. The pathophysiology of portal vein thrombosis in cirrhosis: getting deeper into Virchow's triad. J. Clin. Med. 2022; 11 (3): 800. doi: 10.3390/jcm11030800
2. Chen H., Liu L., Qi X. et al. Efficacy and safety of anticoagulation in more advanced portal vein thrombosis in patients with liver cirrhosis. Eur. J. Gastroenterol. Hepatol. 2016; 28 (1): 82-89. doi: 10.1097/MEG.0000000000000482
3. Loffredo L., Pastori D., Farcomeni A. et al. Effects of anticoagulants in patients with cirrhosis and portal vein thrombosis: a systematic review and meta-analysis. Gastroenterology. 2017; 153 (2): 480-487. doi: 10.1053/j.gastro.2017.04.042
4. Nery F., Chevret S., Condat B. et al. Causes and consequences of portal vein thrombosis in 1243 patients with cirrhosis: results of a longitudinal study. Hepatology. 2015; 61 (2): 660-667. doi: 10.1002/hep.27546
5. Chen H., Turon F., Hernandez-Gea V. et al. Nontumoral portal vein thrombosis in patients awaiting liver transplantation. Liver Transpl. 2016; 22 (3): 352-365. doi: 10.1002/lt.24387
6. de Franchis R., Bosch J., Garcia-Tsao G. et al. Baveno VII — Renewing consensus in portal hypertension. J. Hepatol. 2022; 76 (4): 959-974. doi: 10.1016/j.jhep.2021.12.022
7. Northup P.G., Garcia-Pagan J.C., Garcia-Tsao G. et al. Vascular liver disorders, portal vein thrombosis, and procedural bleeding in patients with liver disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021; 73 (1): 366-413. doi: 10.1002/hep.31646
8. Senzolo M., Sartori M., Rossetto V. et al. Prospective evaluation of anticoagulation and transjugular intrahepatic portosystemic shunt for the management of portal vein thrombosis in cirrhosis. Liver Int. 2012; 32 (6): 919-927. doi: 10.1111/j.1478-3231.2012.02785.x
9. EASL Clinical Practice Guidelines: vascular diseases of the liver. J. Hepatol. 2016; 64 (1): 179-202. doi: 10.1016/j.jhep.2015.07.040
10. Simonetto D.A., Singal A.K., Garcia-Tsao G. et al. ACG Clinical Guideline: disorders of the hepatic and mesenteric circulation. Am. J. Gastroenterol. 2020; 115 (1): 18-40. doi: 10.14309/ajg.0000000000000486
11. Bergere M., Erard-Poinsot D., Boillot O. et al. Portal vein thrombosis and liver cirrhosis: Long-term anticoagulation is effective and safe. Clin. Res. Hepatol. Gastroenterol. 2019; 43 (4): 395-402. doi: 10.1016/j.clinre.2018.11.011
12. Fortea J.I., Carrera I.G., Puente Á. et al. Portal thrombosis in cirrhosis: role of thrombophilic disorders. J. Clin. Med. 2020; 9 (9): 2822. doi: 10.3390/jcm9092822
13. La Mura V., Braham S., Tosetti G. et al. Harmful and beneficial effects of anticoagulants in patients with cirrhosis and portal vein thrombosis. Clin. Gastroenterol. Hepatol. 2018; 16 (7): 1146-1152. doi: 10.1016/j.cgh.2017.10.016
14. Noronha Ferreira C., Reis D., Cortez-Pinto H. et al. Anticoagulation in cirrhosis and portal vein thrombosis is safe and improves prognosis in advanced cirrhosis. Dig. Dis. Sci. 2019; 64 (9): 2671-2683. doi: 10.1007/s10620-019-05572-z
15. Pettinari I., Vukotic R., Stefanescu H. et al. Clinical impact and safety of anticoagulants for portal vein thrombosis in cirrhosis. Am. J. Gastroenterol. 2019; 114 (2): 258-266. doi: 10.1038/s41395-018-0421-0
16. Ghazaleh S., Beran A., Aburayyan K. et al. Efficacy and safety of anticoagulation in non-malignant portal vein thrombosis in patients with liver cirrhosis: a systematic review and meta-analysis. Ann. Gastroenterol. 2021; 34 (1): 104-110. doi: 10.20524/aog.2020.0544
17. Valeriani E., Di Nisio M., Riva N. et al. Anticoagulant treatment for splanchnic vein thrombosis in liver cirrhosis: a systematic review and meta-analysis. Thromb. Haemost. 2021; 121 (7): 867-876. doi: 10.1055/s-0040-1722192
18. Wang L., Guo X., Xu X. et al. Anticoagulation favors thrombus recanalization and survival in patients with liver cirrhosis and portal vein thrombosis: results of a meta-analysis. Adv. Ther. 2021; 38 (1): 495-520. doi: 10.1007/s12325-020-01550-4
19. Zhang Z., Zhao Y., Li D. et al. Safety, efficacy and prognosis of anticoagulant therapy for portal vein thrombosis in cirrhosis: a retrospective cohort study. Thromb J. 2023; 21(1): 13. doi: 10.1186/s12959-023-00454-x.
20. Zhang Z., Zhao Y., Hand B. et al. The efficacy and safety of anticoagulants in the treatment of cirrhotic portal vein thrombosis: a systematic review and meta-analysis. Clin. Appl. Thromb. Hemost. 2022; 28: 10760296221104797. doi: 10.1177/10760296221104797
21. Driever E.G., von Meijenfeldt F.A., Adelmeijer J et al. Nonmalignant portal vein thrombi in patients with cirrhosis consist of intimal fibrosis with or without a fibrin-rich thrombus. Hepatology. 2022; 75 (4): 898-911. doi: 10.1002/hep.32169
22. Guerrero A., Campo L., Piscaglia F. et al. Anticoagulation improves survival in patients with cirrhosis and portal vein thrombosis: The IMPORT competing-risk meta-analysis. J. Hepatol. 2023; 79 (1): 69-78. doi: 10.1016/j.jhep.2023.02.023
23. Gao Z., Li S., Zhao J. et al. Anticoagulation therapy early is safe in portal vein thrombosis patients with acute variceal bleeding: a multi-centric randomized controlled trial. Intern. Emerg. Med. 2023; 18 (2): 513-521. doi: 10.1007/s11739-023-03206-x
24. Zhou T., Sun X., Zhou T. et al. Efficacy and safety of nadroparin calcium-warfarin sequential anticoagulation in portal vein thrombosis in cirrhotic patients: a randomized controlled trial. Clin. Transl. Gastroenterol. 2020; 11 (9): e00228. doi: 10.14309/ctg.0000000000000228.
25. Delgado M.G., Seijo S., Yepes I. et al. Efficacy and safety of anticoagulation on patients with cirrhosis and portal vein thrombosis. Clin. Gastroenterol. Hepatol. 2012; 10 (7): 776-783. doi: 10.1016/j.cgh.2012.01.012
26. Kwon J., Koh Y., Yu S.J. et al. Low-molecular-weight heparin treatment for portal vein thrombosis in liver cirrhosis: Efficacy and the risk of hemorrhagic complications. Thromb. Res. 2018; 163: 71-76. doi: 10.1016/j.thromres.2018.01.032
27. Odriozola A., Puente Á., Cuadrado A. et al. Portal vein thrombosis in the setting of cirrhosis: a comprehensive review. J. Clin. Med. 2022; 11 (21): 6435. doi: 10.3390/jcm11216435
28. EASL Clinical Practice Guidelines on prevention and management of bleeding and thrombosis in patients with cirrhosis. J. Hepatol. 2022; 76 (5): 1151-1184. doi: 10.1016/j.jhep.2021.09.003
29. Han J.M., Koh Y., Kim S.H. et al. Evaluation of low-molecular-weight heparin for treatment of portal vein thrombosis in liver cirrhosis patients. Medicina. 2023; 59 (2): 292. doi: 10.3390/medicina59020292.
30. Cui S.B., Shu R.H., Yan S.P. et al. Efficacy and safety of anticoagulation therapy with different doses of enoxaparin for portal vein thrombosis in cirrhotic patients with hepatitis. Br. Eur. J. Gastroenterol. Hepatol. 2015; 27 (8): 914-919. doi: 10.1097/MEG.0000000000000351
31. Rodriguez-Castro K.I., Vitale A., Fadin M. et al. A prediction model for successful anticoagulation in cirrhotic portal vein thrombosis. Eur. J. Gastroenterol. Hepatol. 2019; 31 (1): 34-42. doi: 10.1097/MEG.0000000000001237
32. Zhang Y., Zhang M., Tan L. et al. The clinical use of Fondaparinux: a synthetic heparin pentasaccharide. Prog. Mol. Biol. Transl. Sci. 2019; 163: 41-53. doi: 10.1016/bs.pmbts.2019.02.004

33. Senzolo M., Piano S., Shalaby S. et al. Comparison of Fondaparinux and low-molecular-weight Heparin in the treatment of portal vein thrombosis in cirrhosis. Am. J. Med. 2021; 134 (10): 1278-1285. doi: 10.1016/j.amjmed.2021.05.013
34. Lu S., Chen J., Zhang R. et al. Comparative effectiveness of warfarin in cirrhotic patients with non-symptomatic portal vein thrombosis: a multicenter, randomized controlled trial. Exp. Rev. Gastroenterol. Hepatol. 2024. doi: 10.1080/17474124.2024.2307575
35. Steffel J., Verhamme P., Potpara T.S. et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Eur. Heart J. 2018; 39 (16): 1330-1393. doi: 10.1093/eurheartj/ehy136
36. Bos S., Schreuder T., Blokzijl H. et al. Anticoagulant activity of edoxaban in patients with cirrhosis. Blood. 2020; 136 (13): 1561-1564. doi: 10.1182/blood.2020005319
37. Shukla A., Giri S. Portal vein thrombosis in cirrhosis. J. Clin. Exp. Hepatol. 2022; 12 (3): 965-979. doi: 10.1016/j.jceh.2021.11.003
38. Biolato M., Paratore M., Di Gialleonardo L. et al. Direct oral anticoagulant administration in cirrhotic patients with portal vein thrombosis: What is the evidence? World J. Hepatol. 2022; 14 (4): 682-695. doi: 10.4254/wjh.v14.i4.682
39. Hum J., Shatzel J.J., Jou J.H. et al. The efficacy and safety of direct oral anticoagulants vs traditional anticoagulants in cirrhosis. Eur. J. Haematol. 2017; 98 (4): 393-397. doi: 10.1111/ejh.12844
40. Nagaoki Y., Aikata H., Daijyo K. et al. Efficacy and safety of edoxaban for treatment of portal vein thrombosis following danaparoid sodium in patients with liver cirrhosis. Hepatol. Res. 2018; 48 (1): 51-58. doi: 10.1111/hepr.12895
41. Hanafy A.S., Abd-Elsalam S., Dawoud M.M. Randomized controlled trial of rivaroxaban vs. warfarin in the management of acute non-neoplastic portal vein thrombosis. Vascul. Pharmacol. 2019; 113: 86-91. doi: 10.1016/j.vph.2018.05.002
42. Ai M.H., Dong W.G., Tan X.P. et al. Efficacy and safety study of direct-acting oral anticoagulants for the treatment of chronic portal vein thrombosis in patients with liver cirrhosis. Eur. J. Gastroenterol. Hepatol. 2020; 32 (10): 1395-1400. doi: 10.1097/MEG.0000000000001846
43. Li A., Zhang M.C., Li P. et al. Direct oral anticoagulants for the treatment of splanchnic vein thrombosis — a systematic review and meta-analysis. Thromb. Res. 2023; 229: 209-218. doi: 10.1016/j.thromres.2023.06.003
44. Koh J.H., Liew Z.H., Ng G.K. et al. Efficacy and safety of direct oral anticoagulants versus vitamin K antagonist for portal vein thrombosis in cirrhosis: a systematic review and meta-analysis. Dig. Liver Dis. 2022; 54 (1): 56-62. doi: 10.1016/j.dld.2021.07.039
45. De Gottardi A., Trebicka J., Klinger C. et al. Antithrombotic treatment with direct-acting oral anticoagulants in patients with splanchnic vein thrombosis and cirrhosis. Liver Int. 2017; 37 (5): 694-699. doi: 10.1111/liv.13285
46. Semmler G., Pomej K., Bauer D.J. M. et al. Safety of direct oral anticoagulants in patients with advanced liver disease. Liver Int. 2021; 41 (9): 2159-2170. doi: 10.1111/liv.14992
47. Serper M., Weinberg E.M., Cohen J.B. et al. Mortality and hepatic decompensation in patients with cirrhosis and atrial fibrillation treated with anticoagulation. Hepatology. 2021; 73 (1): 219-232. doi: 10.1002/hep.31264
48. Menichelli D., Ronca V., Di Rocco A. et al. Direct oral anticoagulants and advanced liver disease: a systematic review and meta-analysis. Eur. J. Clin. Invest. 2021; 51 (3): e13397. doi: 10.1111/eci.13397
49. Nisly S.A., Mihm A.E., Gillette C. et al. Safety of direct oral anticoagulants in patients with mild to moderate cirrhosis: a systematic review and meta-analysis. J. Thromb. Thrombolysis. 2021; 52 (3): 817-827. doi: 10.1007/s11239-021-02424-4
50. Werner K.T., Sando S., Carey E.J. et al. Portal vein thrombosis in patients with end stage liver disease awaiting liver transplantation: outcome of anticoagulation. Dig. Dis. Sci. 2013; 58 (6): 1776-1780. doi: 10.1007/s10620-012-2548-y
51. Nicoara-Farcau O., Soy G., Magaz M. et al. New insights into the pathogenesis, risk factors, and treatment of portal vein thrombosis in patients with cirrhosis. Semin. Thromb. Hemost. 2020; 46 (6): 673-681. doi: 10.1055/s-0040-1715473
52. Boike J.R., Thornburg B.G., Asrani S.K. et al. North American practice-based recommendations for transjugular intrahepatic portosystemic shunts in portal hypertension. Clin. Gastroenterol. Hepatol. 2022; 20 (8): 1636-1662. doi: 10.1016/j.cgh.2021.07.018
53. Prakash S., Bies J., Hassan M. et al. Portal vein thrombosis in cirrhosis: a literature review. Front. Med. 2023; 10: 1134801. doi: 10.3389/famed.2023.1134801
54. Zhang J.B., Chen J., Zhou J. et al. Systematic review and meta-analysis of trans-jugular intrahepatic portosystemic shunt for cirrhotic patients with portal vein thrombosis. World J. Clin. Cases. 2021; 9 (19): 5179-5190. doi: 10.12998/wjcc.v9.i19.5179
55. Zhang D.B., Zhang K.W., Lu D.H. et al. Analysis of the short-and medium-term curative effect of TIPS approach combined with AngioJet thrombus aspiration technology treatment in acute portal vein thrombosis. Zhonghua. Gan. Zang. Bing. Za. Zhi. 2021; 29 (8): 754-758. doi: 10.3760/cma.j.cn501113-20200804-00435
56. Sun X.-Y., Wang G.-C., Wang J. et al. Transjugular intrahepatic portosystemic shunt is effective in patients with chronic portal vein thrombosis and variceal bleeding. Hepatobiliary Pancreat. Dis. Int. 2021; 20 (2): 128-136. doi: 10.1016/j.hbpd.2020.12.016
57. Rodrigues S.G., Sixt S., Abraldes J.G. et al. Systematic review with meta-analysis: Portal vein recanalisation and transjugular intrahepatic portosystemic shunt for portal vein thrombosis. Aliment Pharmacol. Ther. 2019; 49 (1): 20-30. doi: 10.1111/apt.15044
58. Valentin N., Korrapati P., Constantino J. et al. The role of transjugular intrahepatic portosystemic shunt in the management of portal vein thrombosis: a systematic review and meta-analysis. Eur. J. Gastroenterol. Hepatol. 2018; 30 (10): 1187-1193. doi: 10.1097/MEG.0000000000001219
59. Lv Y., Bai W., Li K. et al. Anticoagulation and transjugular intrahepatic portosystemic shunt for the management of portal vein thrombosis in cirrhosis: a prospective observational study. Am. J. Gastroenterol. 2021; 116 (7): 1447-1464. doi: 10.14309/ajg.0000000000001194
60. Zhan C., Prabhu V., Kang S.K. et al. Comparison of non-tumoral portal vein thrombosis management in cirrhotic patients: TIPS versus anticoagulation versus no treatment. J. Clin. Med. 2021; 10 (11): 2316. doi: 10.3390/jcm10112316
61. Lv Y., Qi X., He C. et al. Covered TIPS versus endoscopic band ligation plus propranolol for the prevention of variceal rebleeding in cirrhotic patients with portal vein thrombosis: a randomized controlled trial. Gut. 2018; 67 (12): 2156-2168. doi: 10.1136/gutjnl-2017-314634
62. Wu W., Zhang H., Zeng Z. et al. Comparison of transjugular intrahepatic portosystemic with endoscopic treatment plus anticoagulation for esophageal variceal bleeding and portal vein thrombosis in liver cirrhosis. Scand. J. Gastroenterol. 2022; 57 (12): 1494-1502. doi: 10.1080/00365521.2022.2094724
63. Guo F.F., Wu Z.Y., Zhou P.L. et al. Transjugular intrahepatic portosystemic shunt for the treatment cavernous transformation of the portal vein with vareceal bleeding. Zhonghua Yi Xue Za Zhi. 2020; 100: 387-390. doi: 10.3760/cma.j.issn.0376-2491.2020.05.014

64. Thornburg B., Desai K., Hickey R. et al. Pretransplantation portal vein recanalization and transjugular intrahepatic portosystemic shunt creation for chronic portal vein thrombosis: final analysis of a 61-patient cohort. J. Vasc. Interv. Radiol. 2017; 28 (12): 1714-1721. doi: 10.1016/j.jvir.2017.08.005
65. Thornburg B., Desai K., Hickey R. et al. Portal vein recanalization and transjugular intrahepatic portosystemic shunt creation for chronic portal vein thrombosis: technical considerations. Tech. Vasc. Interv. Radiol. 2016; 19 (1): 52-60. doi: 10.1053/j.tvir.2016.01.006
66. Jiang T.T., Luo X.P., Sun J.M. et al. Clinical outcomes of transcatheter selective superior mesenteric artery urokinase infusion therapy vs transjugular intrahepatic portosystemic shunt in patients with cirrhosis and acute portal vein thrombosis. World J. Gastroenterol. 2017; 23: 7470-7477. doi: 10.3748/wjg.v23.i41.7470
67. Liu K., Li W.D., Du X.L. et al. Comparison of systemic thrombolysis versus indirect thrombolysis via the superior mesenteric artery in patients with acute portal vein thrombosis. Ann. Vasc. Surg. 2017; 39: 264-269. doi: 10.1016/j.avsg.2016.06.029
68. Di Nisio M., Valeriani E., Riva N. et al. Anticoagulant therapy for splanchnic vein thrombosis: ISTH SSC Subcommittee Control of Anticoagulation. J. Thromb. Haemost. 2020; 18 (7): 1562-1568. doi: 10.1111/jth.14836
69. Villa E., Cammà C., Marietta M. et al. Enoxaparin prevents portal vein thrombosis and liver decompensation in patients with advanced cirrhosis. Gastroenterology. 2012; 143 (5): 1253-1260. doi: 10.1053/j.gastro.2012.07.018
70. Kawanaka H., Akahoshi T., Itoh S. et al. Optimizing risk stratification in portal vein thrombosis after splenectomy and its primary prophylaxis with antithrombin III concentrates and danaparoid sodium in liver cirrhosis with portal hypertension. J. Am. Coll. Surg. 2014; 219: 865-874. doi: 10.1016/j.jamcollsurg.2014.07.939
71. Bai D.S., Xia B.L., Zhang C. et al. Warfarin versus aspirin prevents portal vein thrombosis after laparoscopic splenectomy and azygoportal disconnection: a randomized clinical trial. Int. J. Surg. 2019; 64: 16-23. doi: 10.1016/j.ijsu.2019.02.018
72. Elhosseiny S., Al Moussawi H., Chalhoub J.M. et al. Direct oral anticoagulants in cirrhotic patients: current evidence and clinical observations. Can. J. Gastroenterol. Hepatol. 2019; 2019: 4383269. doi: 10.1155/2019/4383269
73. Fu Y., Zhu W., Zhou Y. et al. Non-vitamin K antagonist oral anticoagulants vs. Warfarin in patients with atrial fibrillation and liver disease: a meta-analysis and systematic review. Am. J. Cardiovasc. Drugs. 2020; 20 (2): 139-147. doi: 10.1007/s40256-019-00369-x
74. Hoolwerf E.W., Kraaijpoel N., Buller H.R. et al. Direct oral anticoagulants in patients with liver cirrhosis: a systematic review. Thromb. Res. 2018; 170: 102-108. doi: 10.1016/j.thromres.2018.08.011
75. Huang Z.C., Li C.Q., Liu X.Y. et al. Efficacy and safety of direct oral anticoagulants in patients with atrial fibrillation and liver disease: a meta-analysis and systematic review. Cardiovasc. Drugs Ther. 2021; 35 (6): 1205-1215. doi: 10.1007/s10557-020-07065-y
76. Shatzel J., Dulai P.S., Harbin D. et al. Safety and efficacy of pharmacological thromboprophylaxis for hospitalized patients with cirrhosis: a single-center retrospective cohort study. J. Thromb. Haemost. 2015; 13 (7): 1245-1253. doi: 10.1111/jth.13000
77. Yerke J., Bauer S.R., Bass S. et al. Effectiveness of venous thromboembolism prophylaxis in patients with liver disease. World J. Hepatol. 2019; 11 (4): 379-390. doi: 10.4254/wjh.v11.i4.379
78. Montalvá E., Rodríguez-Perálvarez M., Blasi A. et al. Consensus statement on hemostatic management, anticoagulation, and antiplatelet therapy in liver transplantation. Transplantation. 2022; 106 (6): 1123-1131. doi: 10.1097/TP.0000000000004014

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