Advances in Clinical Medicine 临床医学进展, 2020, 10(3), 185-190
Published Online March 2020 in Hans. http://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2020.103030

Hans汉斯

Research Progress on Etiology of Cirrhosis with Portal Vein Thrombosis

Qian Liu, Wen Han*

Yan'an University Affiliated Hospital, Yan'an Shanxi
Email: lqgogoon@163.com, *6462278364@qq.com

Received: Feb. 17th, 2020; accepted: Mar. 3rd, 2020; published: Mar. 10th, 2020

Abstract

Portal vein thrombosis (PVT) as a very common complication in the natural course of cirrhosis, its incidence is related to the degree of cirrhosis. With the development of diagnostic methods and increasing awareness of clinicians, PVT is better known. This article will review the research progress on the etiology of liver cirrhosis with portal vein thrombosis. The purpose is to further deepen the clinician's understanding of PVT and help to screen out effective indicators that can be used for clinical detection to better prevent and diagnose PVT.

Keywords

Liver Cirrhosis, Portal Vein Thrombosis, Etiology Studies, Progress

肝硬化合并门静脉血栓病因研究进展

刘　倩，韩　文*

延安大学附属医院，陕西　延安
Email: lqgogoon@163.com, *6462278364@qq.com

收稿日期：2020年2月17日；录用日期：2020年3月3日；发布日期：2020年3月10日

摘　要

门静脉血栓(Portal vein thrombosis, PVT)是肝硬化自然进程中很常见的并发症，其发病率与肝硬化程度相关。随着诊断手段的发展及临床医生意识的提高，PVT更多被人熟知。本文将就肝硬化合并门静脉血栓病因相关研究进展作一综述，旨在进一步加深临床医生对PVT的认识，有助于筛选出可用于临床检测的有效指标，更好地进行PVT的预防及诊治。

*通讯作者。

文章引用: 刘倩, 韩文. 肝硬化合并门静脉血栓病因研究进展[J]. 临床医学进展, 2020, 10(3): 185-190.
DOI: 10.12677/acm.2020.103030

关键词

肝硬化，门静脉血栓，病因研究，综述

1. 引言

门静脉血栓(Portal vein thrombosis, PVT)是指在门静脉主干(Portal vein, PV)或其主要分支内形成的血栓，其范围可延伸至脾和肠系膜上静脉(Superior mesenteric vein, SMV)，最终可致门静脉血流部分或完全阻塞。因其形成的程度及速度不同，PVT 的临床表现跨度较大。急性 PVT 通常会出现剧烈的腹部症状，可表现为腹痛、腰部疼痛、肠充血或肠缺血、胃肠道出血、肠梗阻、败血症等；慢性 PVT 通常表现为门静脉高压症(Portal hypertension, PH)，在形成良好侧支循环的患者中可能完全没有症状[1] [2]。PVT 是肝硬化(Liver cirrhosis, LC)自然进程中很常见的并发症，其患病率与肝硬化程度息息相关。在无肝硬化人群中，PVT 不常见，其发病率尚不清楚；在肝硬化代偿期患者中，PVT 患病率可低于 1%；在肝硬化失代偿期患者中，其患病率可高达 25% [3] [4]。近年来也有学者提出肝硬化病因对 PVT 发生率也有影响。有数据表明，非酒精性脂肪性肝炎(Nonalcoholic steatohepatitis, NASH)可能是失代偿性肝硬化住院患者发生严重血栓事件(包括 PVT)的独立危险因素[5] [6]。因为它与纤溶酶原激活物抑制剂的增加和蛋白 C 的水平降低有关[6]。自身免疫性肝炎(Autoimmune hepatitis, AIH)也与肝硬化患者的 PVT 发展密切相关。一项研究发现，在 AIH 继发的肝硬化患者中，有 55%在肝移植时进行了 PVT，而在其他原因引起的肝硬化患者中则为 12% [7]。PVT 首次报道于 1868 年，患者为一名 20 岁男性，临床表现为腹水、脾大、食管静脉曲张(Esophageal varices, EV) [8]。此后，随着诊断手段的发展及临床医生意识的提高，PVT 更多被人认识及重视。PVT 的病因目前仍尚不完全清楚，现将近年来相关病因研究归纳总结，了解其发生机制、影响因素，加深临床医生对此类疾病的认识、提高警惕性，患者亦可从中受益。

2. 病因

Virchow triad 是导致包括 PVT 在内的血栓栓塞事件的 3 种已知病理生理因素，即静脉淤积、高凝状态和内皮功能异常[9]。PVT 的发生通常与上述三要素均有复杂的相关性，并非一种要素可以解释。但为了较明晰解释其相关性，我们仍将其粗略分为三部分进行阐述。

2.1. 静脉淤积

1) 静脉淤积是指继发于肝内结构紊乱的门静脉主干淤积。通常认为在 PVT 形成中，静脉淤积起着主要作用。研究表明，门静脉血流速度 < 15 cm/s 是肝硬化中 PVT 发展最有影响力的危险因素，此数据也通过其他研究得以证明[10] [11]。

2) 侧支血管的形成也可导致静脉淤积。研究表明，在病毒性肝硬化患者中，当其形成流量 > 400 ml/min、流速 > 10 cm/s 形成的侧支血管时，其 PVT 形成风险较未形成此规模侧支循环的患者高[12]，此现象也被称为“偷窃综合征”。

3) 一些针对肝硬化的治疗方法也会导致静脉淤积。非选择性β受体阻滞剂(Non-selective beta blockers,

NSBBs)广泛用于肝硬化患者中食管胃底静脉曲张破裂出血的一级预防及二级预防，NSBBs 会致 PV 流速降低，从而在一定程度上导致静脉淤积。但目前关于 NSBBs 与 PVT 发展的关系存在矛盾的结果。有研究报道 EV 和 NSBBs 暴露是 PVT 发生的危险因素[13] [14]。然而，在另一项证实了 CTP B 级、CTP C 级、肝细胞癌、上消化道出血、PVT 病史及年龄偏大患者中 PVT 患病率明显增加的研究中，尚未报道 PVT 与 NSBBs 治疗之间的相关性[15]。尽管上述结果存在矛盾，但综合来看，PVT 的最根本原因可能仍与更晚期的肝病相关，而随着肝病的进展，NSBBs 被使用到的几率增大。这可能提示 PVT 与 NSBBs 的相关性更多是治疗方案的缘故，而并不是 NSBBs 药物本身的作用。经球囊导管阻塞下逆行闭塞静脉曲张术(Balloon-occluded retrograde transvenous obliteration, BRTO)是一种针对门脉高压引发的静脉曲张的介入治疗方式，现越来越多地应用于临床。BRTO 可有效消除门体分流，从而减少了门脉系统的流出，导致静脉停滞和血栓形成，在接受该手术的患者中，有多达 15%的患者可见到上述现象[16]。故 BRTO 也被认为是门静脉血栓形成的局部危险因素之一。

2.2. 高凝状态

血液的高凝状态，是指血液比正常情况下更易发生凝固的状态。针对患者体内高凝状态形成原因不同，我们将从系统性因素、局部性因素及其他相关因素三方面予以阐述。

2.2.1. 系统性因素

系统性因素包括遗传性血友病(如因子 V Leiden 突变、蛋白 C 或 S 缺乏症、抗凝血酶缺乏症)、骨髓增生异常、怀孕和口服避孕药。有研究显示骨髓增生性疾病(Myeloproliferative neoplasms, MPN)和遗传性血栓形成是 PVT 的最常见的系统危险因素[17]。

MPN 患者动脉血栓和静脉血栓的风险均增加[18] [19]。MPN 中血栓形成是一个复杂且多方面的过程，涉及血小板、红细胞、白细胞和内皮细胞的数量及功能的改变[18]。在 MPN 患者中可发生 JAK2V617F 突变。从病理生理学的角度来看，JAK2V617F 突变似乎通过 P-选择蛋白的过表达导致血栓形成，从而导致血小板聚集、纤维蛋白沉积[20] [21]。另一项研究表明，约有一定比例的 PVT 肝硬化患者具有继发于 JAK2V617F 突变的骨髓增生性疾病[22]。

血友病(主要是 V Leiden 因子、凝血酶原 G20210A 和 JAK2V617F 突变)可能是另一个危险因素。在各种血栓形成性遗传缺陷中，G20210A 凝血酶原基因变异是 LC 患者最常见的与 PVT 相关的异常，PVT 的患病率为 21.4%~29%，比值比为 5.9 [23] [24]。

2.2.2. 局部性因素

基于血小板减少症的存在和常规凝血试验的延长，传统上认为肝硬化患者肝细胞功能下降，凝血功能不佳，更易出血，但近年来，越来越多的研究提示，肝硬化患者体内的凝血抗凝系统维持了一个较低的平衡，且此平衡极易被打破，从而导致高凝状态。最近的数据显示，由于高因子 VIII/蛋白 C 变化、凝血酶生成增加及血红蛋白改变，机体易产生获得性血栓形成前状态，这可能会增加血栓形成的风险[25] [26] [27]。Ambrosino P.等人的一项临床研究结果也证实这些实验数据提示肝硬化患者静脉血栓栓塞风险增加，PVT 患病率约 10% [28]。

我们需要进一步研究以确定这些参数是否可用于日常临床实践中以预测 LC 中 PVT 的发生[29] [30]。

2.2.3. 其他因素

其他不为人知的外源性因素可能在上述血栓形成原因的背景下起作用。

最近的研究提示，肝硬化晚期因细菌从肠腔内转移至门脉而导致的低级内毒素血症可能是凝血系统的潜在诱因，目前已证明肠道微生物群中的脂多糖可增加内皮细胞 VIII 因子的释放，即内毒素血症为促

血栓形成的触发因素[31]。尽管内毒素血症与肝硬化中凝血酶生成的标志物之间存在明显相关性，但一项包含 49 位肝硬化患者的临床研究尚未能证明内毒血症与 PVT 形成之间的相关性[32] [33]。因此我们应在更大的研究中广泛探讨内毒素血症在门静脉循环中的潜在作用。

另外，上文所提到的 NASH 也正在成为 PVT 的潜在危险因素，因为它与纤溶酶原激活物抑制剂的增加和蛋白 C 的水平降低有关[6]。

2.3. 内皮功能异常

由于直接的血管损伤和血流紊乱，EV 内镜治疗、腹部手术(包括脾切除)、炎症、外伤以及肿瘤细胞侵袭血管(如肝癌、胆管癌、其他部位癌症肝转移)均被认为是 PVT 的潜在影响因素。此前曾有报道指出腹部手术和脾切除术为 PVT 的危险因素。特别是，在一项涉及 113 例无恶性肝硬化患者的回顾性研究中，脾切除术使 PVT 发生风险增加 10 倍，而与肝功能障碍的严重程度无关[34] [35] [36]。

此外，EV 内镜治疗与 PVT 的相关性目前仍尚不明确，一项平均随访期为 16 个月的前瞻性研究显示，已有 16%的肝硬化患者(70%伴有血栓性疾病)在接受 EV 内镜治疗后出现 PVT [23]；然而另一项前瞻性研究未能证明在接受硬化剂治疗 EV 的肝硬化患者中 PVT 发生风险增加[37]。故今后仍需大量大数据样本研究，从而明确两者相关性，为 PVT 的防治提供新思路。

3. 结论与展望

PVT 的形成与多种因素相关，临床医生应深刻认识此类疾病，提高警惕性，选择合理诊疗方案。此外，目前对是否可通过相关因素检测来预估 PVT 形成风险、评价 PVT 病变程度仍尚无定论，这有赖于更多前瞻性研究及更大规模的回顾性研究的开展。

参考文献

[1] Sheen, C.L., Lamparelli, H., Milne, A., Green, I. and Ramage, J.K. (2000) Clinical Features, Diagnosis and Outcome of Acute Portal Vein Thrombosis. *QJM*, **93**, 531-534. https://doi.org/10.1093/qjmed/93.8.531

[2] Condat, B., Pessione, F., Helene Denninger, M., Hillaire, S. and Valla, D. (2000) Recent Portal or Mesenteric Venous Thrombosis: Increased Recognition and Frequent Recanalization on Anticoagulant Therapy. *Hepatology*, **32**, 466-470. https://doi.org/10.1053/jhep.2000.16597

[3] Francoz, C., Belghiti, J., Vilgrain, V., *et al*. (2005) Splanchnic Vein Thrombosis in Candidates for Liver Transplantation: Usefulness of Screening and Anticoagulation. *Gut*, **54**, 691-697. https://doi.org/10.1136/gut.2004.042796

[4] Okuda, K., Ohnishi, K., Kimura, K., *et al*. (1985) Incidence of Portal Vein Thrombosis in Liver Cirrhosis. An Angiographic Study in 708 Patients. *Gastroenterology*, **89**, 279-286. https://doi.org/10.1016/0016-5085(85)90327-0

[5] Stine, J.G., Argo, C.K., Pelletier, S.J., Maluf, D.G., Caldwell, S.H. and Northup, P.G. (2017) Advanced Non-Alcoholic Steatohepatitis Cirrhosis: A High-Risk Population for Pre-Liver Transplant Portal Vein Thrombosis. *World Journal of Hepatology*, **9**, 139-146. https://doi.org/10.4254/wjh.v9.i3.139

[6] Stine, J.G., Shah, N.L., Argo, C.K., Pelletier, S.J., Caldwell, S.H. and Northup, P.G. (2015) Increased Risk of Portal Vein Thrombosis in Patients with Cirrhosis Due to Nonalcoholic Steatohepatitis. *Liver Transplantation*, **21**, 1016-1021. https://doi.org/10.1002/lt.24134

[7] Ruiz, P., Sastre, L., Crespo, G., *et al*. (2017) Increased Risk of Portal Vein Thrombosis in Patients with Autoimmune Hepatitis on the Liver Transplantation Waiting List. *Clinical Transplantation*, **31**, e13001. https://doi.org/10.1111/ctr.13001

[8] Balfour, G.W. and Stewart, T.G. (1869) Case of Enlarged Spleen Complicated with Ascites, Both Depending upon Varicose Dilatation and Thrombosis of the Portal Vein. *Edinburgh Medical Journal*, **14**, 589-598.

[9] Chawla, Y.K. and Bodh, V. (2015) Portal Vein Thrombosis. *Journal of Clinical and Experimental Hepatology*, **5**, 22-40. https://doi.org/10.1016/j.jceh.2014.12.008

[10] Zocco, M.A., Di Stasio, E., De Cristofaro, R., Novi, M., Ainora, M.E., Ponziani, F., Riccardi, L., Lancellotti, S., Santoliquido, A., Flore, R., Pompili, M., Rapaccini, G.L., Tondi, P., Gasbarrini, G.B., Landolfi, R. and Gasbarrini, A. (2009) Thrombotic Risk Factors in Patients with Liver Cirrhosis: Correlation with MELD Scoring System and Portal Vein

Thrombosis Development. *Journal of Hepatology*, **51**, 682-689. https://doi.org/10.1016/j.jhep.2009.03.013

[11] Stine, J.G., Wang, J., Shah, P.M., Argo, C.K., Intagliata, N., Uflacker, A., Caldwell, S.H. and Northup, P.G. (2018) Decreased Portal Vein Velocity Is Predictive of the Development of Portal Vein Thrombosis: A Matched Case-Control Study. *Liver International*, **38**, 94-101. https://doi.org/10.1111/liv.13500

[12] Maruyama, H., Okugawa, H., Takahashi, M. and Yokosuka, O. (2013) De Novo Portal Vein Thrombosis in Virus-Related Cirrhosis: Predictive Factors and Long-Term Outcomes. *American Journal of Gastroenterology*, **108**, 568-574. https://doi.org/10.1038/ajg.2012.452

[13] Nery, F., Correia, S., Macedo, C., Gandara, J., Lopes, V., Valadares, D., Ferreira, S., Oliveira, J., Gomes, M.T., Lucas, R., Rautou, P.E., Miranda, H.P. and Valla, D. (2019) Nonselective Beta-Blockers and the Risk of Portal Vein Thrombosis Inpatients with Cirrhosis: Results of a Prospective Longitudinal Study. *Alimentary Pharmacology & Therapeutics*, **49**, 582-588. https://doi.org/10.1111/apt.15137

[14] Zampino, R., Lebano, R., Coppola, N., Macera, M., Grandone, A., Rinaldi, L., De Sio, I., Tufano, A., Stornaiuolo, G., Adinolfi, L.E., Durante-Mangoni, E., Battista, G.G. and Niglio, A. (2018) The Use of Nonselective Beta Blockers Is a Risk Factor for Portal Vein Thrombosis in Cirrhotic Patients. *Saudi Journal of Gastroenterology*, **24**, 25-29. https://doi.org/10.4103/sjg.SJG_100_17

[15] Violi, F., Corazza, G.R., Caldwell, S.H., Perticone, F., Gatta, A., Angelico, M., Farcomeni, A., Masotti, M., Napoleone, L., Vestri, A., Raparelli, V. and Basili, S. (2016) Portal Vein Thrombosis Relevance on Liver Cirrhosis: Italian Venous Thrombotic Events Registry. *Internal and Emergency Medicine*, **11**, 1059-1066. https://doi.org/10.1007/s11739-016-1416-8

[16] Yoshimatsu, R., Yamagami, T., Tanaka, O., *et al*. (2012) Development of Thrombus in a Systemic Vein after Balloon-Occluded Retrograde Transvenous Obliteration of Gastric Varices. *Korean Journal of Radiology*, **13**, 324-331. https://doi.org/10.3348/kjr.2012.13.3.324

[17] DeLeve, L.D., Valla, D.-C. and Garcia-Tsao, G. (2009) Vascular Disorders of the Liver. *Hepatology*, **49**, 1729-1764. https://doi.org/10.1002/hep.22772

[18] Barbui, T., Finazzi, G. and Falanga, A. (2013) Myeloproliferative Neoplasms and Thrombosis. *Blood*, **122**, 2176-2184. https://doi.org/10.1182/blood-2013-03-460154

[19] Falanga, A. and Marchetti, M. (2012) Thrombotic Disease in the Myeloproliferative Neoplasms. *Hematology—American Society of Hematology Education Program*, **2012**, 571-581. https://doi.org/10.1182/asheducation.V2012.1.571.3798557

[20] Arellano-Rodrigo, E., Alvarez-Larrán, A., Reverter, J.C., Villamor, N., Colomer, D. and Cervantes, F. (2006) Increased Platelet and Leukocyte Activation as Contributing Mechanisms for Thrombosis in Essential Thrombocythemia and Correlation with the JAK2 Mutational Status. *Haematologica*, **91**, 169-175.

[21] Robertson, B., Urquhart, C., Ford, I., *et al*. (2007) Platelet and Coagulation Activation Markers in Myeloproliferative Diseases: Relationships with JAK2 V6I7 F Status, Clonality, and Antiphospholipid Antibodies. *Journal of Thrombosis and Haemostasis*, **5**, 1679-1685. https://doi.org/10.1111/j.1538-7836.2007.02626.x

[22] Saugel, B., Lee, M., Feichtinger, S., Hapfelmeier, A., Schmid, R.M. and Siveke, J.T. (2015) Thrombophilic Factor Analysis in Cirrhotic Patients with Portal Vein Thrombosis. *The Journal of Thrombosis and Thrombolysis*, **40**, 54-60. https://doi.org/10.1007/s11239-014-1124-z

[23] Amitrano, L., Brancaccio, V., Guardascione, M.A., Margaglione, M., Sacco, M., Martino, R., De Nucci, C., Mosca, S., Iannaccone, L., Ames, P.R., Romano, L. and Balzano, A. (2002) Portal Vein Thrombosis after Variceal Endoscopic Sclerotherapy in Cirrhotic Patients: Role of Genetic Thrombophilia. *Endoscopy*, **34**, 535-538. https://doi.org/10.1007/s11239-014-1124-z

[24] Erkan, O., Bozdayi, A.M., Disibeyaz, S., Oguz, D., Ozcan, M., Bahar, K., Karayalcin, S., Ozden, A., Bozkaya, H., Yurdaydin, C. and Uzunalimoglu, O. (2005) Thrombophilic Gene Mutations in Cirrhotic Patients with Portal Vein Thrombosis. *European Journal of Gastroenterology & Hepatology*, **17**, 339-343. https://doi.org/10.1097/00042737-200503000-00013

[25] Tripodi, A., Primignani, M., Chantarangkul, V., *et al*. (2009) An Imbalance of Pro- vs Anti-Coagulation Factors in Plasma from Patients with Cirrhosis. *Gastroenterology*, **137**, 2105-2111. https://doi.org/10.1053/j.gastro.2009.08.045

[26] Gatt, A., Riddell, A., Calvaruso, V., Tuddenham, E.G., Makris, M. and Burroughs, A.K. (2010) Enhanced Thrombin Generation in Patients with Cirrhosis-Induced Coagulopathy. *Journal of Thrombosis and Haemostasis*, **8**, 1994-2000. https://doi.org/10.1111/j.1538-7836.2010.03937.x

[27] Hugenholtz, G.C., Macrae, F., Adelmeijer, J., *et al*. (2016) Procoagulant Changes in Fibrin Clot Structure in Patients with Cirrhosis Are Associated with Oxidative Modifications of Fibrinogen. *Journal of Thrombosis and Haemostasis*, **14**, 1054-1066. https://doi.org/10.1111/jth.13278

[28] Ambrosino, P., Tarantino, L., Di Minno, G., *et al*. (2017) The Risk of Venous Thromboembolism in Patients with

Cirrhosis. A Systematic Review and Meta-Analysis. *Thrombosis and Haemostasis*, **117**, 139-148. https://doi.org/10.1160/TH16-06-0450

[29] Lancellotti, S., Basso, M., Veca, V., Sacco, M., Riccardi, L., Pompili, M. and De Cristofaro, R. (2016) Presence of Portal Vein Thrombosis in Liver Cirrhosis Is Strongly Associated with Low Levels of ADAMTS-13: A Pilot Study. *Internal and Emergency Medicine*, **11**, 959-967. https://doi.org/10.1007/s11739-016-1467-x

[30] Mikuła, T., Kozłowska, J., Stańczak, W., Sapuła, M., Różyk, A. and Wiercińska-Drapało, A. (2018) Serum ADAMTS-13 Levels as an Indicator of Portal Vein Thrombosis. *Gastroenterology Research and Practice*, **2018**, Article ID: 3287491. https://doi.org/10.1155/2018/3287491

[31] Carnevale, R., Raparelli, V., Nocella, C., Bartimoccia, S., Novo, M., Severino, A., De Falco, E., Cammisotto, V., Pasquale, C., Crescioli, C., Scavalli, A.S., Riggio, O., Basili, S. and Violi, F. (2017) Gut-Derived Endotoxin Stimulates Factor VIII Secretion from Endothelial Cells. Implications for Hypercoagulability in Cirrhosis. *Journal of Hepatology*, **67**, 950-956. https://doi.org/10.1016/j.jhep.2017.07.002

[32] Violi, F., Ferro, D., Basili, S., Lionetti, R., Rossi, E., Merli, M., Riggio, O., Bezzi, M. and Capocaccia, L. (1997) Ongoing Prothrombotic State in the Portal Circulation of Cirrhotic Patients. *Thrombosis and Haemostasis*, **77**, 44-47. https://doi.org/10.1055/s-0038-1655904

[33] Wosiewicz, P., Żorniak, M., Hartleb, M., Barański, K., Hartleb, M., Onyszczuk, M., Pilch-Kowalczyk, J. and Kyrcz-Krzemień, S. (2016) Portal Vein Thrombosis in Cirrhosis Is Not Associated with Intestinal Barrier Disruption or Increased Platelet Aggregability. *Clinics and Research in Hepatology and Gastroenterology*, **40**, 722-729. https://doi.org/10.1016/j.clinre.2016.03.008

[34] Amitrano, L., Guardascione, M.A., Brancaccio, V., Margaglione, M., Manguso, F., Iannaccone, L., Grandone, E. and Balzano, A. (2004) Risk Factors and Clinical Presentation of Portal Vein Thrombosis in Patients with Liver Cirrhosis. *Journal of Hepatology*, **40**, 736-741. https://doi.org/10.1016/j.jhep.2004.01.001

[35] Bagheri Lankarani, K., Homayon, K., Motevalli, D., Heidari, S.T., Alavian, S.M. and Malek-Hosseini, S.A. (2015) Risk Factors for Portal Vein Thrombosis in Patients With Cirrhosis Awaiting Liver Transplantation in Shiraz, Iran. *Hepatitis Monthly*, **15**, e26407. https://doi.org/10.5812/hepatmon.26407

[36] Qi, X., Han, G., Ye, C., Zhang, Y., Dai, J., Peng, Y., Deng, H., Li, J., Hou, F., Ning, Z., Zhao, J., Zhang, X., Wang, R. and Guo, X. (2016) Splenectomy Causes 10-Fold Increased Risk of Portal Venous System Thrombosis in Liver Cirrhosis Patients. *Medical Science Monitor*, **22**, 2528-2550. https://doi.org/10.12659/MSM.898866

[37] Politoske, D., Ralls, P. and Korula, J. (1996) Portal Vein Thrombosis Following Endoscopic Variceal Sclerotherapy. Prospective Controlled Comparison in Patients with Cirrhosis. *Digestive Diseases and Sciences*, **41**, 185-190. https://doi.org/10.1007/BF02208603