Chapter

Gastroduodenal Lesions Associated with Portal Hypertension: An Extensive Review

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Abstract

The block of the portal flow by obstacles in prehepatic, hepatic or posthepatic site and alterations of the splanchnic blood flow are the pathological conditions that lead to portal hypertension. The portal hypertension can cause also others gastroduodenal lesions, potentially hemorrhagic, in addition to esophageal varices commonly developed and habitual source of bleeding in these patients. The gastroduodenal lesions associated with portal hypertension, usually encountered in the clinical practice, are portal hypertensive gastropaty, gastric antral vascular ectasia, gastric and duodenal ulcer, isolated gastric varices. The pathophysiology and clinical, diagnostic and therapeutic features of these lesions are examined.

Keywords: portal hypertension, portal hypertensive gastropathy, gastric antral vascular ectasia, peptic ulcer bleeding, gastric varices

1. Introduction

Hepatic fibrosis, nodular rigeneration, distortion of hepatic architecture are the histopathological characters of liver cirrhosis. The main outcome of this pathological condition is the portal hypertension (PH) by the disruption of the hepatic blood flow, beside the damage of liver metabolic functions. Moreover the alteration of the splanchnic blood flow and the block of portal flow can be localized also in the prehepatic and posthepatic site. The prehepatic causes of PH are portal vein thrombosis, splenic vein thrombosis, arteriovenous fistula, blood overflow in the splanchnic district; the posthepatic causes are the Budd-Chiari syndrome, inferior vena cava obstruction, right-sided heart failure [1]. The liver cirrhosis is a remarkable medical problem in the world. Cirrhosis and hepatic chronic diseases are an important cause of morbidity and mortality worldwide, but with many differences in the geographic distribution. The global mortality rate ranges from 2% to 4% of total deaths in 2017, with decrease from the rate variance 1%–9%, evaluated in 1990 [2]. The more evident clinical evolutions of liver cirrhosis are PH, damage of coagulation, digestive hemorrhage, ascites, hepatic encephalopathy, hepatocarcinoma.

2. PH related gastroduodenal lesions

The PH leads to some pathological conditions in the esophageal and gastroduodenal tract, that can cause digestive hemorrhage. Esophageal varices are the lesion currently developed in the patients with PH by liver cirrhosis or other pre and posthepatic obstacles to splanchnic blood flow. Consequently in these patients all gastrointestinal bleedings are usually ascribed to esophageal varices. Instead others gastroduodenal lesions, potentially hemorrhagic, can be associated with PH. In this group of lesions there are the portal hypertensive gastropathy (PHG), gastric antral vascular ectasia (GAVE), gastric and duodenal ulcer, isolated gastric varices. The aim of this presentation is to evaluate the development, the clinical prominence and therapeutic needs of these lesions, which are associated but also conditioned by PH.

2.1 Portal hypertensive gastropaty

Varices are activated collateral vessels and they develop following the obstruction of portal flow. The role of activation of collateral vessel is to allow the retourn of digestive portal blood flow into the systemic circulation. PHG has similarly its cause in the obstruction in portal flow. All PHG occur in patients with PH, but not all patients with PH can develop PHG. The PHG was previously called as hemorrhagic gastritis within the large group which includes many bleeding gastric pathologies; later it was correctly framed and defined in the context of complications of PH. The clinical observation shows that the patients with severe PH and longer liver disease duration with esophageal varices, expecially if treated with endoscopic procedures, have more frequently PHG. In the gastric mucosa there are congestion and dilated capillaries [3]. The hemodynamic changes of the PH, caused by some mechanical and functional obstacles to portal circulation, as hepatic cirrhosis, pre or posthepatic block, portal hyper-inflow, are the pathophysiological basis of PHG. The congestion of the gastric mucosa is the first phenomenon of the obstruction of the portal flow. The most important question is whether and in which way can occur the change in hematic perfusion of the stomach during PH. The etiology of PHG is not completely known. In the PH there is an important hemodinamic characteristic, that is a hyperdynamic circulation based on the increased hematic flow in the mesenteric, splenic and total gastric sections. The hyperdynamic circulation is one factor which induces the PHG, based on the changes in blood flow of gastric mucosa [4]. The hyperdynamic characteristcs in the PH lead to some important hemodynamic changes in the patients. In the hyperdynamic circulation of PH intrahepatic vascular resistence greaten, whereas mean arterial pressure and systemic vascular resistence reduce and there is wide vasodilatation in the splanchnic sector. Finally the gastric blood flow is globally increased, but the particular gastric mucosal flow should be reduced [5]. The gastric mucosal blood flow, in the patients with PHG, is now discussed. Some studies report decreased gastric mucosal blood flow [6], but these data can be modified, as increase of mucosal blood flow, after correction of PH, for example by TIPS [7]. There are other studies that underline, on the contrary, the increase of gastric mucosal blood flow [8]. Clinical observation in PHG shows major tendency to actions of gastrotoxic substances and decreased wound healing. Consequently the more obvious clinical appearance of PHG is the gastrointestinal bleeding, usualy of mild or moderate entity and diffuse from the gastric wall. Ultimately the hemodynamic changes cause the impairments of gastric mucosal defense competence with major sensitivity to injuries and alteration of growth factors, with minor possibility of mucosal healing [9]. Synthetically the weak gastric mucosa more easily can bleed and reduced mucosal

blood perfusion, with altered gastric microcirculation leads to increased sensitivity to hypoxia and noxions agent, with erosion, ulcers and bleeding. PHG is related to severity of liver cirrhosis and in particular is connected with the increase degree of hepatic vein pressure gradient (HVPG). PHG is a dinamic condition because in its evaluation can occur some reversible gastric mucosal changes [10]. PHG incidence raises with increasing of hypertension in the portal area and is associated with esophageal and gastric varices; it's a strong predictor of gastroesophageal varices bleeding [11]. In fact PHG occur frequently in patients with liver cirrhosis and its major incidence is based on the severity of PH. This lesion can modify its degree from midl to severe and can disappear. Bleeding can occur but is not frequent and often of not serious entity. The role of sclerotherapy of esophageal varices on the natural history of PHG is not unanimously defined. Following some experience, the treatment of esophageal varices does not seem to influence the evolution of PHG, but there are others observations opposite to this hipothesis in the literature [12]. PH develops direct action on gastric mucosa. The PHG encompasses a large types of gastric mucosal lesions in the cirrhotic patients. These lesions should be distinguished from others lesions as GAVE, which is an independent pathology. These following modifications shape the PHG. About gastric mucosal hemodinamic changes, it's not clear if gastric mucosal hyperhemia is by active or passive hemodynamic congestion. In the pathogenesis of PHG there are together the action of increase of the portal pressure and of gastric blood flow (hyperdynamic splanchnic circulation) which causes its development. Moreover in PHG there is the damage of gastric mucosal defense factors, with the occurrence of bleeding, that is its unique clinical manifestation [13]. In the pathogenesis of PHG can be identified some steps. The hemodynamic changes in the splanchnic district and in particular in the stomach are caused by increased portal pressure. The most evident modification is the congestion in the gastric wall, with the tissue impairment. Consequently there is the activation of cytokines and growth factors (TNF alfa) and subsequent activation of endothelial constitutive nitric oxide (NO) synthase in the gastric mucosa. The increased presence of NO synthase produces excess of NO which leads to hyperdinamic circulation and overproduction of peroxinitrite, that induces, with endothelin, the major susceptibility of gastric mucosa to injuries [14]. There are controversial data in the literature on the kind of changes of gastric mucosa blood flow: in some studies there is the increase but in others there is decrease of blood flow. In summary remain unclear if hemodynamic changes in PHG are active or passive congestion [15, 16]. Others observations suggest that cirrhotics with PHG have increased gastric perfusion but without congestion. The magnitude of changes in gastric perfusion and the endoscopic severity of PHG had no relationship with the degree of PH [17]. In the patiens with liver cirrhosis can occur both gastric lesions, PHG and GAVE. These pathologies have different pathophysiology and management. They have the same clinical manifestations as gastric bleeding, usually chronic but in some cases the gastric hemorrhage can be acute and with high entity. The endoscopic diagnosis for differentiation can be difficult and the histology can be useful [18]. The endoscopic appearance of the PHG is characteristic: flushed and edematous mucosa that suggest mosaic pattern, dilated mucosal and submucosal vessels without inflammation. Further evolutions of these lesions are friable mucosa which bleeds easily on contact and there are hemorrhagic spots. The site of these pathological mucosal lesions can occur frequently in the proximal stomach, but the same lesions by mesenteric hypertension can be observed in others sections of the gastrointestinal tract [3]. Histological features of PHG are dilated, congested capillaries, edema, extravasated red blood cells (RBCs), smooth muscle hyperplasia [19]. Further special problem is the connection of PHG with infection of Helicobacter pylori (H.pylori). Some data from the literature report that

infection prevalence of H.pylori in cirrhotic patients with PHG is lower than general population [20]. The diminution of H.pylori infection in cirrhotic patients should be related to the gastric vascular congestion characteristic of PHG [21]. Mucosal gastric changes in PH are characterized by the alteration of mucus protection, that become slimmer, riduction of gastric acidity based on minor acid secretion, decrease of Prostaglandin with lowered gastric blood flow and impaired gastric barrier. The alteration of gastric mucosal barrier is worsened by severe impairment of gastric wall microcirculation, with the result of vascular congestion, followed by mucosal hypoxia and reduction of oxigen released in gastric mucosa. In summary the debility of gastric mucosal barrier of PHG could make easy mucosal lesions and infectious invasion, e.g. by H.pylori. However the vascular congestion, impaired microcirculation and mucosal hypoxia in PHG allow the increase of intestinal metaplasia of gastric mucosa, which is an opposed element to H.pylory infection [22]. In summary, based on these data of the literature, a current evaluation suggest that the minor H.pylori infection rate in cirrhotic patients with PHG can be connected to intestinal metaplasia of gastric mucosa [23]. Clinical presentation of PHG is the gastrointestinal bleeding. The hemorrhage can present as acute or chronic complication. The frequence of acute bleeding shows a wide range from 2% to more than 40% in various reports [12, 24, 25]. The great variance of frequency can be due to vast time frame of references and to difficulties and imprecisions of endoscopic examination during acute bleeding in congiunction with others potential source hemorrhage as esophageal varices. In summary the endoscopic diagnosis can be sure only if the bleeding point is identified [26]. The acute bleeding in PHG usually, almost 90% of cases, can occur in the patients with advanced cirrhosis, longer duration and major extension and severity of gastropathy. The extent of bleeding in the PHG is usually mild or moderate [27, 28]. Very difficult is the evaluation of the incidence of chronic bleeding from PHG, that frequently can be mild. Some references of the literature report the frequence variation that oscillates between 3%–26% [29]. In fact there are many uncertainties in the definition of chronic bleeding as which level of hemoglobin reduction, but, most important, the coexistent clinical condition of anemia in cirrhotic patients, also without gastrointestinal bleeding. The diagnosis of PHG is only endoscopic. Some endoscopic features have been identified as diagnostic: snake skin, stripped appearance, mild reddening mosaic in the mild appearance of gastropathy; flat red spots, fine red speckling mosaic characterize the endoscopic appearance of moderate disease; finally the more severe condition of gastropathy can be identified in the diffuse hemorrhagic lesions, red spots, point bleeding mosaic. This summary of some classifications proposal of endoscopic features of PHG shows the discordance among various experience reported in the literature, about shared definitions and identifications for each endoscopic lesion of PHG [13, 25, 30]. Most frequently the detection of asymptomatic PHG occur during endoscopic control of esophageal varices in the patients with chronic liver disease. In these patients there is not appearance of gastrointestinal bleeding and you can say that PHG developed spontaneusly. In the evolution of PHG should be evaluated the role of the treatment of esophageal varices by sclerotherapy or ligation. Some data of the literature refer an increased occurrence of PHG following endoscopic therapy of esophageal varices. In this perspective should be proposed prophylactic pharmacotherapy with nonselective betablockers as propranolol. In summary for asymptomatic PHG is usually not required treatment [28, 31]. If the PHG is recognized as the cause of anemia due to chronic bleeding, drug therapy can be started with iron replacement, in some cases blood transfusion and drugs that can lower the pressure in the portal district as betablocker propranolol. In the cases of acute bleeding the first procedures are for the resuscitation of the patient with blood transfusion, vasoconstrictors as

somatostatin or analogues and antibiotics. It's suddenly mandatory the endoscopic control of esophageal varices and possible their treatment if bleeding. When there is the endoscopic certainty of PHG as source of acute hemorrhage, should be possible the use of endoscopic therapy also for PHG and the current pharmacotherapy by betablocker propranolol, somatostatin or analogues, vasopressin. In the rare cases of acute hemorrhage not responded to medical therapy can be requested emergency therapy with TIPS [18]. Endoscopic therapy of PHG has been proposed with the use of the laser, but the results are uncertain and consequently it has been little used. All the drugs employed in the management of PHG, connected with hypertensive condition in the portal district are based on the reduction of gastric blood flow and gastric perfusion [3].

2.2 Gastric antral vascular ectasia

Gastric antral vascular ectasia (GAVE) occurs roughly in the 30% of the patients with cirrhosis [32]. Two types of GAVE syndrome, with different natural history and clinical features, can be identified. The non- cirrhotic GAVE syndrome in particurar is associated to autoimmune diseases, more frequently in aged women, with Rainaud's syndrome, sclerodactyly, atrofic gastritis [33]. Beside association with various autoimmune diseases, there are, in non-cirrhotic GAVE syndrome, the pathological association with sclerodermia, chronic renal failure, etc. [34]. The etiology of GAVE syndrome is now yet undefined and the pathogenesis of vascular characteristic alterations as ectasia should by contracted by mechanical actions on the gastric mucosa. This hypothesis is based on some histological characteristics, in particular the fibromuscolar hyperplasia, as results of mechanical actions [35]. The histologic features of GAVE can be summarized with the following data: prevalent presence of the lesions in the antrum, vascular ectasia, submucosal fibrohyalinosis, spindle cells (smooth muscle cell – myofibroblast hyperplasia) proliferation, fibrin thrombi in mucosal vessells [36, 37]. The GAVE syndrome shows the characteristic endoscopic appearance of watermelon stomach, gastric dilation, linear lesions localized in the antrum, vasodilation and tendency to the bleeding. Endoscopic features of GAVE are represented by conglomerates of red spots which are organized in a linear pattern in the gastric antrum, taking shape of watermelon stomach. Following the pathogenetical proposal of Lowes J R, can be evaluated the role of neuroendocrine cells proliferations in GAVE and effect of its vasoactive intestinal peptide on vessels wall with vascular ectasia [38]. The occurrence of GAVE in the patients with liver cirrhosis should be due to the obstacle of the portal flow, consequent PH, spontaneous shunting of mesenteric flow through collateral vessells, as esophageal varices, and impaired hepatic catabolism of some vasoactive substances [35]. The management of GAVE syndrome is not well established in all clinical manifestations. The central aim of the therapeutic procedures is the control of the bleeding, that occurs more frequently in GAVE than in PHG, usually as chronic gastrointestinal hemorrhage, in cirrhotic patients with clinical appearance of chronic anemia. The chronic anemia is a clinical condition that belongs to liver cirrhosis and can be also caused by PHG; for this reason the differential diagnosis of the causes of anemia is necessary to prepare specific therapies [18]. Some procedures have been employed: medical therapies with estrogen and progesterone, tranexamic acid (antifibrinolitic substance), octreotide, propranolol. All these medical treatments showed partial therapeutic effectiveness, therefore, if the ineffective medical therapies, can be accessed to invasive surgical therapies for control of hypertensive condition in mesenteric district, as TIPS or to direct treatment of hemorrhagic source with antrectomy. Unfortunately the surgical procedures in cirrhotic patients can be connected with not negligeable

risk of morbidity and mortality [35, 39–41]. In the treatment of GAVE have been employed endoscopic procedures based on thermoablative techniques. In particular argon plasma coagulation and Nd:Yag laser coagulation. For these procedures usually should be repeated some sessions. Cryotherapy has been used with rapid expansion in the stomach of compressed nitroux oxide and following freezing of the mucosa, allowing therapeutic effect on diffuse lesions [42–44]. In the final evaluation we can conclude that endoscopic approach with thermoablative procedures as argon plasma coagulation, Nd:Yag laser coagulation and cryotherapy have advantagious therapeutic effects on decrease of bleeding and needs of blood transusion in complicated hemorrhagic GAVE [18]. In summary PHG and GAVE are potential hemorrhagic mucosal lesions of the stomach that can develop in the patients with PH by liver cirrhosis. Both pathologies can cause more frequently chronic or sometime acute gastrointestinal bleeding. Therefore these conditions have some pathological and clinical differences. The PHG occur only in cirrhotics with PH, the hemorrhagic lesions are located mostly in the gastric fundus and the pharmacological therapies are frequently effective. The GAVE can be also present in the patients without liver cirrhosis and PH (60%–70% of the cases), the gastric site of the lesions is antrum almost always, there is the histological characteristic of fibrin thrombi in the mucosal vessells and signs of mucosal inflammation, finally the therapeutic procedures are endoscopic (argon, laser, cryotherapy).

2.3 Gastric and duodenal ulcer

Another lesions, possible source of upper gastrointestinal bleeding in cirrhotic patients are the peptic ulcers, located in duodenum and stomach. The frequency of bleeding from gastroduodenal ulcers in cirrhotics, rather than from esophageal varices ranges from 5% to 15% [45, 46]. Gastroduodenal peptic ulcer disease maintains a not negligeable prevalence in the general population that reaches 14% [47]. The etiology and natural history of peptic ulcer pathology is connected and conditioned by certain well known factors: mainly environmental, behavioral and infectious, as the infection of H.pylori, curative use of NAIDS, etc. However the role of associated pathologies cannot be left out. In fact liver cirrhosis carries an enlarged risk of occurrence of peptic ulcer disease with the incidence that varies widely from 10% to 49% [48]. The pathophysiological connections among peptic ulcer disease, liver cirrhosis with metabolic changes related and infection of H.pylori are object of numerous studies. Especially the prevalence of H.pylori infection in cirrhotic patients is reported in the various researches with great variability and this does not allow to define if the H.pylori infection has a specific role in the pathogenesis of ulcerative disease in cirrhotics. For example in some studies the high incidence of peptic ulcer in the patients with liver cirrhosis is associated also to great presence of H.pylori infection until 60% of cases [49]. On the other hand there are many studies which refer the prevalence rates of H.pylori infection in cirrhotics not dissimilar compared to the values of non cirrhotic patients [50]. Ultimately the data on the role of H.pylori about the occurrence and development of peptic ulcer during chronic liver disease are debatable and in conclusion uncertain; in any case it's not evident a significant action of H.pylori infection in the pathophysiology of peptic ulcer disease in the cirrhotic patients. Therefore in summary we can believe that there are no significant differences in the prevalence of H.pylori infection between general population and patients with chronic liver disease [50]. Neverthless this observation, it can be accepted that peptic ulcers develop more frequently in the cirrhotic patients. The clinical appearances of peptic ulcers in cirrhotic patients are characterized by negative features of ulcer disease evolution as greater frequence of bleeding and recurrence of the disease

and retarded recovery. The reason of greater occurrence of peptic ulcers is based on the modification of gastric-acid secretion, changed gastric mucosal blood flow and, mostly, on damaged mucosal defense mechanisms. In fact there is not evidence of increase of gastric-acid secretion in cirrhotic patients with PH and, on the contrary, the possible variations are almost always as hypocloridric changes likely related to worsening of liver disease [51]. The damaged protective function of gastric mucosal barrier seems to have a greater role in the pathophysiology of peptic ulcers in cirrhotics, based on the occurrence of chronic atrophyc gastritis in liver cirrhosis, the reduced strength of gastric mucosa due to parietal venous congestion and protein and vitamin deficiencies [52]. Others metabolic and functional modifications should integrate the pathogenetic framework of peptic ulcer in cirrhotic patients: raised level of gastrin and histamine, increase of duodenogastric reflux, impaired gastric empting, reduced prostaglandin level in gastric mucosa and decrease of mucosal oxigen saturation [53, 54]. Most recent studies confirm this proposal evaluation referring that the severity degree of liver pathological involvement plays an important role in the development of peptic ulcer disease. Decompensated cirrhosis, the action of PH, more effective if more serious, on gastric mucosal blood flow, on efficiency of mucosal defense barrier and on epithelial resumption, can support ulcer development, the retard of mucosal recovery and possible recurrence of peptic disease [50, 55]. In summary in the pathophysiology of peptic ulcer in cirrhotics, the H.pylori infection and NSAID therapeutic use are risk factors with effects no different than in the general population. However in the patients with cirrhosis and PH, in which peptic ulcer disease occur with notable percentage, the liver pathology operates a significant pathogenetic role [56]. The prevalence of peptic ulcer in cirrhotics is more high compared with general population, both in symptomatic patients with bleeding and in asymptomatic patients [57]. There is a greater prevalence of peptic ulcer disease in cirrhotic patients and these patients have major risk of bleeding from peptic ulcer related to general population; moreover each occurrence of peptic ulcer bleeding is followed by the decompensation of hepatic cirrhosis with increase of severity of clinical conditions [58, 59]. In the patients with liver cirrhosis upper gastrointestinal bleeding is currently reported to esophageal varices, but in the 30% -40% of cases the source of bleeding is not esophageal varices but gastroduodenal ulcers, with subsequent remarkable morbidity and mortality [60]. Upper gastrointestinal bleeding is the common and expected complication of liver cirrhosis with PH. The first therapeutic purpose is to control the hypovolemic alterations of various degrees of severity due to amount of hemorrhage and to steady the hemodynamic conditions. The subsequent step requires by diagnostic approach to differentiate the bleeding from esophageal varices or from others gastroduodenal pathologies connected to hepatic cirrhosis, as peptic ulcers. The hemodynamic instability requires resuscitation, that can be restrictive or aggressive, by infusion of cristalloids (Ringer lactate, normal saline, etc.) or also, in some cases, of colloids (albumin, plasma, dextrane, etc.). If the indication is found can be useful the use of blood transfusion. In the first therapeutic approach the evaluation of bleeding severity encompasses also the assessment of level of the risk of rebleeding in order to graduate the subsequent phases of treatment using Glasgow Blatchford score [61]. The severe gastrointestinal hemorrhage from ulcer lesions in cirrhotic patients adversely affects the prognosis through worsening of already impaired liver functions. In the patients with upper gastrointestinal bleeding from peptic ulcers the therapeutic perspective is based on the pharmacologic treatment that includes the use of proton pump inhibitors, somatostatin and octreotide, and on the endoscopic diagnostic definition and management. The endoscopic therapies, with hemostatic purpose, include various procedures as epinephrine injection, thermocoagulation, sclerosant injection, use

of the clips, TC-325 Hemospray. The global management of non variceal upper gastrointestinal bleeding has been recently defined by international guideline [62]. Finally in case of failure of pharmacologic and endoscopic management of peptic ulcers in cirrhotics and serious unmanageable clinical conditions, could be proposed direct surgical gastroduodenal procedures as rescue therapy.

2.4 Isolated gastric varices

Gastric varices are usually connected with esophageal varices, but can be also isolated along the gastric wall. Gastric varices are classified by endoscopy with topographical criterion as gastroesophageal varices type I (lesser gastric curvature), gastroesophageal varices type II (greater gastric curvature); isolated gastric varices type I (gastric fundus), isolated gastric varices type II (any stomach location, except fundus) [63]. The pathogenesis of isolated gastric varices could be ascribed to portal or splenic vein thrombosis. The occurrence of bleeding from isolated gastric varices in the patients with PH shows the percentage incidence from 5% to 10% [64]. The diagnosis of gastric varices is endoscopic. The first general therapeutic approach in the case of bleeding from gastroesophageal or isolated gastric varices is included within the current management of gastrointestinal hemorrhage in the PH, by pharmacological and endoscopic procedures, or portosystemic derivation procedures as TIPS. The specific treatment of isolated gastric varices bleedind is endoscopic usually by injection with cyanoacrylate [65].

3. Conclusions

In the clinical scenario of gastroduodenal lesions associated with PH and liver cirrhosis, both are important actors, but the PH and hepatic chronic disease remain the protagonist of the clinical state. In fact the degree of functional hepatic impairment and of hypertensive status in the splanchnic district affect much the patients general conditions. Moreover the upper gastrointestinal bleeding is the more frequent complication of this complex pathological condition. Esophageal varices currently develop in the cirrhotics with PH and this is the characteristic source of gastrointestinal bleeding. However upper digestive hemorrhage in cirrhotic patients alwais requires the diagnostic definition of bleeding source, which may also be due to pathologies related to PH. In fact, albeit less frequently, others gastroduodenal lesions, with pathogenetic association to liver cirrhosis and PH, may present intestinal hemorrhage. The PHG is in several cases neglected complication of liver cirrhosis and PH. PHG is connected with the degree of PH and can have a role as prognostic index of liver cirrhosis. The management of PHG is based on pharmacological, endoscopic or, in some few cases, on emergency therapy with TIPS. GAVE can affect one third of cirrhotics. PHG and GAVE may both occur in patients with liver cirrhosis. However these pathologies have different pathophysiology and management. The central diagnostic aim is to distinguish GAVE from PHG because the therapeutic procedures that allow decrease of portal pressure, effective for PHG, are not efficacious therapy for GAVE, usually treated by endoscopic approach. Gastric and duodenal ulcer are more frequent in cirrhotics and may worsen prognosis. Early diagnosis and treatment of peptic ulcer in cirrhotic patients are significant to avoid complications. Gastric varices, usually connected with esophageal varices, can be, in some cases, isolated; their therapeutic approach in case of bleeding is enclosed within the effective management of gastrointestinal hemorrhage in the PH. In conclusion the complete diagnosis that identifies with certainty, the bleeding source is decisive for the therapeutic choices.

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