www.englishproofread.com

Academic Proofreading Services Ltd.
Unit 1a, Park Farm Road, Folkestone,
Kent, United Kingdom CT19 5EY
Company no.: 8433468
Email: contact@englishproofread.com

CERTIFICATE OF PROOFREADING

Certificate date: **3rd November 2022**

English Proofread ref.: **20221031_AK_9123**

Issued to: **Admir Kurtcehajic**

This certificate is provided as confirmation that the paper below has been proofread by **English Proofread**. The final word count after proofreading is 4,067 and the **proofread manuscript is attached below** for your reference.

Neither the research content nor the intentions of the author(s) were altered in any way during the proofreading process.

English Proofread guarantees the quality of the English language in this paper, provided our proofreader's changes are accepted and no further changes were made after the document was checked by our proofreader. Please note that where the proofreader has added a comment suggesting a revision or indicating uncertainty about the meaning of any part of the text, **English Proofread** cannot guarantee the standard of English for those highlighted sections.

Please address any queries to contact@englishproofread.com or to view our services, please go to http://www.englishproofread.com/international-academics/.

Abstract

A portal vein aneurysm (PVA) is abnormal focal dilation of the portal vein and is defined as a portal vein diameter exceeding 19 mm in cirrhotic patients and 15 mm in a normal liver. A PVA as an abnormality of the portal venous system was first reported in 1956 by Barzilai and Kleckner. A review from 2015 entitled "*Portal vein aneurysm: What to know*" considered fewer than 200 cases. In the last seven years, there has been an increase in the number of PVAs diagnosed thanks to routine abdominal imaging. The aim of this review is to provide a comprehensive update of the situation regarding PVAs, including aetiology, epidemiology and clinical assessment, along with an evaluation of advanced multimodal imaging features of aneurysms and management approaches.

Key words: aneurysm, portal vein, abdominal imaging, treatment, follow-up

Deleted: P
Deleted: the
Deleted: the
Deleted: ly was
Deleted: R
Commented [NK1]: The authors may just want to say ...200 cases... as this is given as the figure later on.
Deleted: "
Deleted: "
Deleted: l
Deleted: ss
Deleted: 7
Deleted: id
Deleted: nt
Deleted: of
Deleted: ha
Deleted: s bee
Deleted: rai
Deleted: the
Deleted: ing
Deleted: u
Deleted: from all aspect
Deleted: the
Deleted: ,
Deleted: ,
Deleted: furthermore
Deleted:
Deleted:

Core tip

Portal vein aneurysms are rare vascular abnormalities, representing 3% of all venous aneurysms in the human body, and they are not well understood. They can be congenital or acquired, located mainly at the level of confluence, main trunk, branches and bifurcation. In this review, analysing available literature data, novelties in all aspects of these visceral venous abnormalities are presented (including aetiology, epidemiology, clinical assessment, imaging and treatment).

Introduction to PVAs

A portal vein aneurysm (PVA) is a focal saccular abnormality or fusiform dilatation of the portal venous system, and it is defined as a portal vein (PV) diameter exceeding 19 mm in cirrhotic patients and 15 mm in a normal liver. PVAs are rare vascular abnormalities, representing 3% of all venous aneurysms in the human body, and they are not well understood [1–7].

Douglass et al. studied 92 autopsies and reported that the diameter of the PV was between 0.64 mm and 12.1 mm in patients without cirrhosis and those without portal hypertension [8]. In 1976, Doust et al. conducted a vascular study of 53 patients to assess the size of the PV and underlying liver status through abdominal ultrasound, and they detected that the maximum calibre of the PV was 19 mm in cirrhotic patients and 15 mm in patients with normal livers. Hence, a portal vein diameter of >20 mm is universally regarded as the threshold for diagnosis of a PVA [9].

In a retrospective study by Koc et al., involving 4186 patients who had undergone routine abdominal contrast-enhanced computed tomography (CT), the prevalence of PVAs was 0.43% [10]. The location of a PVA can be extrahepatic or intrahepatic. Extrahepatic PVAs often occur in the main trunk of the PV, the splenomesenteric confluence at the level of the PV bifurcation, the main branches of the PV, the splenic vein (SV) and the superior mesenteric vein (SMV). A study by Doust et al. characterized intrahepatic PVAs as having a diameter measuring more than 7 mm in normal patients and 8.5 mm in cirrhotic patients [9]. PVAs as abnormalities of the portal venous system were first reported in 1956 by Barzilai and Kleckner [11]. A review from 2015 entitled "*Portal vein aneurysm: What to know*" considered 96 reports and included 190 patients [1].

Aiming to clarify novelty as regards these visceral vascular abnormalities, we performed a literature search of the PubMed database for all articles relating to PVAs between January 2015 and July 2022. We collected 57 reports, involving 62 patients with a PVA [3–7, 12–16, 19, 21–25, 27, 29–68]; we also found one retrospective study with 18 PVA patients [2], and three cases of PV pseudoaneurysms [69, 70, 71].

Epidemiological characteristics

Deleted: T

Formatted: Space After: 8 pt, Line spacing: 1.5 lines

Deleted: i… are rare vascular abnormalitiesy… representing 3% of the …ll venous aneurysms in the ¶ human body, and they areis…not well understood. TheyIt…canould…be congenital or acquired, located mainly at the level of confluence, main trunk, branches and bifurcation. In this review, analysing available literature data, novelties in all aspects of these visceral venous abnormalities are presented (including aetiology, epidemiology, clinical assessment, imaging and treatment) of this visceral venous abnormality are presented …

Formatted: Space After: 0 pt

Deleted: f

Deleted: ¶ P…rtal vein aneurysm (PVA) is the …bnormal…focal saccular abnormality or fusiform dilatation of the portal venous system, and it is defined as a portal vein (PV) diameter exceeding the …9 mm in cirrhotic patients and 15 mm in a normal liver. PVA It i… are rare vascular abnormalitiesy… representing 3% of the …ll venous aneurysms in the human body, and they areis…not well understood [1–– …

Deleted: to…12.1 mm in patients without cirrhosis and those without portal hypertension [8]. In 1976, Doust et al. cC…nducted a vascular study am…fng…53 patients to assess the size of the PV and underlying liver status through abdominal ultrasound, and they detected that the …aximum calibrer… …

Deleted: R…trospective study by Koc et al., involvinged…4186 patients who had undergone routine abdominal contrast-enhanced computed tomography (CT), the prevalence of PVAs was 0.43% [10]. ThR…gards…location of a PVA canould…be extrahepatic orand… …ntrahepatic. ELocation of the e…trahepatic PVAs oftecould be mai…ly…occur in the main trunk of the PV, the splenomesenteric confluence at the,…level of the PV bifurcation, the main branches of the PV, fur…hermore…splenic vein (SV) and the superior mesenteric vein (SMV). A sS…udy by Doust et al. characterized an intrahepatic PVAs as havingf it i…as…diameter measuringes…mola…g…r…than 7 mm in normal patients and 8.5 mm in cirrhotic patients [9]. ¶ PVAs as an …bnormalitiesy…of the portal venous system were firstly…was …eported in 1956 by Barzilai and [11]. A rR…view from 2015 entitled "*"…ortal vein aneurysm: What to know*"… considered 96 reports and,…includeding… …

Deleted: i…e visceral vascular abnormalitiesy… we have performed a literature re…earch of the PubMm…d database for all articles relatinged…to PVAs betweenfrom…January 2015 au…dtil the…July of …022. WIn th… last seven years we have …ollected 57 reports, ico…volvsider…ng 62 patients with a PVA [3–…, 12–…6, 19, 21–…5, 27, 29–– 68]; we additiona…so foundly …one retrospective study with 18 PVA patients [2], and three3…cases ofwith…PV pseuo… …

Of the 62 patients in the review, 33 (53%) were male; the patients were between 1 (youngest) and 95 (oldest) years of age, and the mean patient age at diagnosis was 54.85 years (±21.72). The incidence of reported PVAs per year is shown in *Figure 1*.

In terms of aetiology, the frequency of congenital PVAs was 29 (46.7%), and it was 17 (27.4%) for acquired PVAs. In 16 (25.8%) patients, the aetiology of the PVA was unclear. With regard to the location of PVAs, 27.41% were at the level of the splenomesenteric confluence; 19.35% were at the main trunk; 17.74% were at branches; 6.45% were at the PV bifurcation; 6.45% were at the SV; and 4.83% were at the SMV; 14.51% were classified as intrahepatic PVAs. A retrospective study by Ahmed et al. [2] included 18 patients (13 of whom were female (72.2%)), aged between 20 and 101 years, with an average age of 56 years.

Our review also covered three patients (all male) with a PV pseudoaneurysm resulting from trauma.

Etiopathogenesis

The aetiology of PVAs is not clear. Postulated origins include both congenital and acquired causes. It is well known that the main cause of acquired PVAs is chronic liver disease (cirrhosis and fibrosis) with portal hypertension. Long-standing portal hypertension causes intimal thickening with compensatory medial hypertrophy of the portal vein. Over time, medial hypertrophy is replaced by fibrous tissue, leading to weakening of the vein wall, thus making it susceptible to aneurysmal dilatation [12, 13]. However, the incidence of portal hypertension and PVAs is disproportionate, suggesting the existence of other contributory factors.

Acquired PVAs can also be part of severe pancreatitis, likely to be due to leakage of digestive enzymes, causing localized inflammation of the PV. Other known aetiologies of acquired PVAs are malignancy and trauma [1].

A pseudoaneurysm of the PV is defined as post-traumatic abnormal dilation of the portal venous system. It is a serious condition requiring an interventional approach; five cases were reported in the literature during the period of our review [71]. In relation to a new acquired aetiology of PVAs, the following conditions were noted: Budd-Chiari syndrome [14], splenomegaly in thalassaemia major [15] and giant splenic artery aneurysms [16]. Long-term cholelithiasis was also considered as a possible cause of PVAs [17]. Some PVAs are congenital. During gestation, three pairs of veins are developed: the cardinal veins, umbilical veins and vitelline veins. The PV, hepatic veins and part of the inferior cava vein (ICV) come from umbilical veins and vitelline veins. Generally, cranial segments of the left vitelline vein and caudal segments of the right vitelline vein regress during the foetal period, and the SV and SMV are derived from the left vitelline vein [18].

Deleted: T…e review included …2 patients w…n the review PVA… of whome …3 (53%) were male; the patients w, ag…re between 1 (youngest) au…dtil…95 (oldest) years of age, and,…the mean patient age at diagnosis was 54.,…5 years (±21.,…2). The iI…cidence of reported PVAs per year is showed o… inthe …

Deleted: R…ga…md… ofthe…aetiology, the frequency of congenital PVAs was 29 (46.,…%), and it was 17 (27.4%) for acquired PVA wa… 17 (27,4%)… In 16 (25.,… …) of patients, the aetiology of the PVA was unclear. With rR…gard tos…the location of PVAs, 27.41% were-…at the level of the splenomesenteric confluences was… (27,41%),…19.35% were at the main trunk; (19,35%),…branches (…7.,…4% were at branches;),…6.45% were at the PV bifurcation; (6,45%),…SV (….,…5% were at the SV;),…and SMV (….,…3% were at the SMV)… (…4.,…1%)…wereas…classified as an …ntrahepatic PVAs. A rR…trospective study by Ahmed et al. [2] included 18 patients (; …3 of whom were female 13 …72.2%)) … r…n…ed between 20 and – …

Deleted: by

Deleted: ¶

Deleted: ¶
E…iology of PVAs is not clear. P, p…stulated origins include both congenital and acquired causes. It isThe…well known es…hat tblis…e main causes…of the …cquired of …VAs isare…the …hronic liver disease (cirrhosis and, …

Commented [NK2]: The authors may want to say ...the main causes of acquired PVAs are chronic liver disease (cirrhosis and fibrosis) and portal hypertension...

Deleted: With…time, the …edial hypertrophy is replaced bywith…fibrous tissue, leading to a …

Deleted: ould…be …lso be a …art of severe pancreatitis, likely to be due to leakage of digestive enzymes, causing localized inflammation of the PV. Other known aetiologies …

Deleted: P…eudoaneurysm of the PV is defined as a …ost-traumatic abnormal dilation of the portal venous system. I, i… is a seu…iousgent…condition,…requiring anes…interventional approach; literature has reported …ive cases were reported iu… the i…iterature now…during the period of our review [71]. In relation he se…ting …f…a new possible …cquired aetiology of PVAs, nex…he following conditions were noted: Budd-Chiariy…syndrome [14], splenomegaly in thalassaemia major [15] and with …iant splenic artery aneurysms [16]. Long- …erm cholelithiasis was also considered as a possible cause of PVAs [17]. Some PVAs are cC…ngenital PVA… D – d…ring the …estation, three pairs of veins are developed:,…the cardinal veins, the umbilical veins and the …itelline veins. The PV, hepatic veins and part of the inferior cava vein (ICV) come from umbilical veins and vitelline veins. Generally, cranial segments of the left vitelline vein and caudal segments of the right vitelline vein regress during the foetal period, and the SV and the …

Evidence supporting a congenital cause includes reported cases of *in utero* diagnosis of PVAs, evidence of PVAs in patients with histologically proven normal livers (particularly in children and young adults), normal portal venous pressure in the presence of a PVA, and the frequent stability of aneurysms at follow-up imaging. Theories for a congenital cause involve inherent weakness in the vessel wall or incomplete regression of the distal right primitive vitelline vein, leading to a vascular diverticulum that ultimately develops into an aneurysm. Congenital PVAs are usually incidentally diagnosed later in life (not in neonatal or paediatric age groups) when an abdominal ultrasound is carried out because of some other indication [4, 6, 19]. Burdall et al. evaluated the relation between trisomy 21 (Down's syndrome) and congenital vascular malformation of the liver in a study of 45 children, seven of whom had vascular malformation and two of whom had evidence of a PVA [20].

Clinical assessment of patients with a PVA, symptomatology and complications

The symptomatology of PVAs is controversial and poorly understood. According to the review article by Laurenzi et al. [1], 30% of patients with a PVA were asymptomatic, and 50% experienced non-specific abdominal pain. In our review, we found that up to 25% of patients were asymptomatic; for 15% of patients, the authors did not provide clear symptoms relating to the PVA, and approximately 30% of patients experienced non-specific abdominal pain. In patients with a PVA, the nature of non-specific abdominal pain should be clarified. The main question is whether low-pressure PVAs are truly the source of the pain; gastritis, duodenitis and cholecystitis, etc., should be ruled out. A retrospective study by Ahmed et al. [2] showed that in eight (44.4%) patients with abdominal pain, a PVA was actually the source of the pain in only one patient.

Up to 10% of cases involve portal hypertension, gastrointestinal bleeding (varices) or symptoms related to compression of adjacent organs (abdominal swelling or jaundice) [1]. With a PVA, symptoms or complications such as portal hypertension and bleeding are possible. One thing that should be clarified is whether a PVA is a consequence of portal hypertension or whether the PVA is causing portal hypertension. Khan et al. found coexistence of a giant splenic artery aneurysm, portal hypertension without liver cirrhosis and a PVA at the level of bifurcation. In this case, the PVA and portal hypertension were presumed to be secondary to the pressure effect from the splenic artery aneurysm [16]. Güngör et al. presented an 11-month-old girl with a congenital PVA, and oesophageal and fundal varices with bleeding [21]. This was the only case in our review where PVA caused portal hypertension complications.

Symptomatology has a close relation with morphology, size and location of the PVA. When it grows, there can be contact with the biliary tract, the ICV and duodenum, etc., and complications can arise from compression of these organs. Six patients in our review (9.67%) had compression complications, including four biliopathies [22, 23, 24, 25], one thrombosis in the ICV [7] and one intestinal obstruction [19].

Formatted: Font: Italic

Deleted: , …articularly in children and young adults), the presence of …ormal portal venous pressures…in the presetti…ceg…of a PVA, and the frequent stability of aneurysms at follow-up imaging. Theories for a congenital cause involve inherent weakness in the vessel wall or incomplete regression of the distal right primitive vitelline vein, leading to a vascular diverticulum that ultimately develops into an aneurysm. Congenital PVAs areis…usually incidentally diagnosed later in the …ife (not in neonatal or paediatric age groups) when an abdominal ultrasound is carried outne…because ofor…some other indication [4, 6, Burdall et al. evaluated the relation between the …risomy 21 (Down's syndrome) and congenital vascular malformation of the liver in a,…study ofincluded…45 children, where …even of whom7 children…had vascular malformation and,…two of whom children …

Deleted: ¶

Deleted: ¶
S…mptomatology of the …VAs is controversial and poorly understood. According to the review article by Laurenzi et al. [1], 30% of patients with a PVA were asymptomatic, and 50% expei…ienced with …on- …pecific abdominal pain. In our review, we found that up to 25% of patients were asymptomatic;,…for 15% of patients, the authors did no'… provide clear symptoms relatferr…ng to the PVA, and approximately 30% of patients experienced a …on-specific abdominal pain. In those …atients with a PVA, the nature of a …on- …pecific abdominal pain should be clarified. The main question is wheth– do…s PVA, …egards…its …ow-pressure PVAs are truly the source of the pain; gastritis, duodenitis and,… …holecystitis, etct…, should be previosly ruled out. A rR…trospective study by Ahmed et al. [2] showed that …n eight8…(44.,…%) …atients with an abdominal pain, th…t…PVA was actr…ally the source of the pain in only in …

Deleted: cur…involve portal hypertension, gastrointestinal bleeding (varices),…or symptoms related to the compression of adjacent organs (abdominal swelling or,…jaundice) [1]. WiIn …he…asetting of…PVA, symptoms or complications such as portal hypertension and bleeding are posdi…cut…bi…e. One thing that should be clarified , …s whether a PVA is a consequence of the …ortal hypertension,…or whether the PVA is causings…portal hypertension. Khan et al. were …ound to …oexistence of a giant splenic artery aneurysm, portal hypertension without liver cirrhosis and a PVA at the level of bifurcation. In this case, the PVA and portal hypertension were presumed to be secondary to the pressure effect from the splenic artery aneurysm [16]. Güngör et al. presented an 11- …onth-olds…girl with a congenital PVA, afollowi…dg by…oesophageal and fundal varices with bleedie…g [21]. This was the only case in our review where PVA causeding…complication of …

Deleted: i… ain…the …lose relation with morphology, size and location of the PVA. When it grows, there canould…be contact with thea…biliary tract, the ICV and,…duodenum, etc., and complications can arisom… from me…nti…mprn…ssion of thesed…organs due to compression… Six patients in oO…r review covered 6 (9.,…7%) patients wit…ad compression complication of compres…ion… …

Laurenzi et al. reported PVA complications such as thrombosis (which happened in 20% of cases) and a rupture (which occurred twice) [1]. A recent retrospective study by Ahmed et al. [2] reported 18 patients with a PVA; 22.22% of patients had thrombosis, and no ruptures were reported. PVAs with acute portal vein thrombosis are reported in the literature as nearly always being symptomatic, with 91% of patients reporting abdominal pain, 53% reporting fever and 38% presenting with ascites [26].

In our review, thrombosis occurred in 12 (19.35%) patients (six of whom were female), with a median age of 38.33 years. Abdominal pain was reported in 10 of 12 patients; in a one-year-old girl, the symptoms manifested as haematemesis and melena [21]; a 69-year-old female with a congenital PVA did not experience any symptoms [5]. In five patients, treatment was based on anticoagulation medication; seven patients underwent open surgery or invasive radiology procedures. In our review, a rupture as a complication of a PVA was not reported. Patients with a PVA have a series of laboratory tests, including complete blood count, inflammatory parameters, basic metabolic profile and liver function tests.

Imaging

Increased use of abdominal cross-sectional imaging in recent years has led to a growing number of cases describing PVAs, and as such, proper handling of this lesion is increasingly relevant to both diagnostic and interventional radiologists. Evaluation of PVAs by multiple imaging modalities is important because a PVA can mimic solid, cystic or hypervascular abdominal masses [1–7].

Sonography assessments can be performed for differential diagnosis to determine whether anechoic areas or cysts at porta hepatis are PVAs, hepatic artery aneurysms or choledochal cysts. Abdominal ultrasound based on the greyscale of the PVA produces an anechoic structure with a "*smoke effect*" within, which simulates a natural contrast agent, determined by slowed venous flow (*Figure 2a*). Spectral Doppler sonography can reveal the presence of a monophasic, non-pulsatile venous flow pattern inside the aneurysm (*Figure 2b*). With colour Doppler sonography of a PVA, anechoic areas will be completely filled, looking like the Korean flag or a "*yin-yang*" sign. Hepatic artery aneurysms show a colour flow with arterial waveform, but choledochal cysts do not show such colour flow and are connected to biliary channels [6, 15].

Contrast-enhanced CT with angiography shows the filling of PVAs. On a CT and MRI scan, a PVA will appear as a well-defined contrast-enhanced focal saccular anomaly or fusiform dilatation of the portal venous system during the portal venous phase [4, 27].

In one case, CT angiography facilitated better assessment of the portal venous system, which contained some thin calcifications in the aneurysmal wall and the main portal trunk [13]. Iimuro et al. presented "*computational fluid dynamics software*", analysing the haemodynamics of the portal venous system, including congenital saccular PVAs at the level of confluence. Turbulent flow was obvious in PVAs,

Deleted: of PVA…such as thrombosis (which happened in 20% of cases),…and a rupture (which occurrapp…n… two t…cm…s… [1]. A rR…cent retrospective study by Ahmed et al. [2] reported 18 patients with a PVA; thrombosis happened in …2.,…2 … of patients had thrombosis, and no rupture wa… werenot…reported. PVAs with acute portal vein thrombosis,…h…rs b…en…reported in the literature as nearly always being symptomatic, with 91% of patients reporting abdominal pain, 53% reporting fever, …

Deleted: frequency for …hrombosis occurredwas…in 12 (19.,…5%) patients (six, 6…of whom were female), with a median age of 38., …

Commented [NK3]: If the median figure relates just to the female patients, the authors may want to say ...(six of whom were female, with a median age of 38.33 years)...

Deleted: ,…in a one-1 …ear- …ld girl, the symptoms manifested as haematemesis and melena [21];,…a 69- …ear-old female with a congenital PVA did not experienced…any symptoms [5]. In five5…patients, treatment was based on the anticoagulation medication;,…seven7…patients were underwentgo… …

Commented [NK4]: The authors may want to say ...had... if they are referring to the patients in the studies reviewed, rather than general practice.

Deleted: il…ries ofntl…laboratory tests, including complete blood count, inflammatory parameters, basic metabolic profile,… …

Deleted: ¶

Deleted: The g…east…dr…usetilization…of abdominal cross-sectional imaging in recent years has led to a growing number of cases describing PVAs, and as such, proper handling of this lesion is increasingly relevant to …oth diagnostic and interventional radiologists … Evaluation of PVAs by multiple imaging modalities is important because a PVA can mimic solid, cystic,…or hypervascular abdominal masses [1–- …

Deleted: On the s…nography assessments can be performed for differential diagnosis to determinef…whether anechoic areas or cysts at porta hepatis are PVAs, hepatic artery aneurysms orand…choledochal cysts. Abdominal ultrasound based on the grea… …cale of the PVA producei… an anechoic structure with a "*smoke effect*" within, which simulates a natural contrast agent, determined by the …lowed venous flow (*Figure 2a*). Spectral Doppler …onography can rd…vemonstr…lting…the presence of a monophasic, non-pulsatile venous flow pattern inside the aneurysm (*Figure 2b*). WiOn …he…colour Doppler sonography of a PVA, has a complete filling of an …nechoic areas will be completely filled, i…ookingt appears…like the " …

Deleted: "…or a "y*Y…n- …Y…ng*" sign. Hepatic artery aneurysms show a colour flow with arterial waveform, but choledochal cysts do not show such colour flow and h…res…commu…nei…a…edi…ton with …

Formatted: Font: Not Italic

Deleted: …n a CT and MRI scan, a PVA wills…appr…ci…rted…as a well-defined contrast- …

Deleted: low…d a …etter assessment of the portal venous system, wt…ichat…contained some thin calcifications in the aneurysmal wall and the main portal trunk [13]. Iimuro et a …

and the wall shear stress against the upper-posterior part of the aneurysm wall was greater than in other parts of the aneurysm. In order to prevent the PVA from growing and avoid thrombosis or a rupture, an aneurysmectomy of the PVA was performed [28].

The diagnostic role of endoscopic ultrasound (EUS) was highlighted in congenital PVAs at the level of the splenomesenteric confluence. EUS confirmed the presence of anechoic lesions adjacent to the neck of the pancreas [29]. EUS as a diagnostic tool was also used for assessment of an intrahepatic aneurysmal portosystemic venous shunt [30].

"*Intraductal ultrasonography*" (IDU) was used for the first time to identify an adjacent PVA as the cause of a common hepatic duct stricture, showing a lobulated hypoechoic mass containing a mobile echogenic substance, outside of the biliary tract, highly suggestive of a vascular lesion [24].

Management and treatment of PVAs

Because of their rarity, the natural history of PVAs remains unclear, and the optimal strategy for management is controversial. Following diagnosis of a PVA, treatment will depend on the size, symptoms and location of the PVA, and comorbidities.

If the PVA is asymptomatic (as in 30% of cases), it does not require any active treatment, and monitoring (a policy of "wait and see") should be adopted [1]. While asymptomatic aneurysms smaller than 30 mm can be clinically observed, surgical intervention may be necessary in large asymptomatic aneurysms (>30 mm) [10]. The origin, morphology and symptomatology of a PVA, along with comorbidities and conservative treatment, are shown in *Table 1*.

Where there is thrombosis due to a PVA, anticoagulation treatment should be considered. In a recently published case, a 10-year-old boy with PVA thrombosis was treated with enoxaparin. The thrombosis disappeared completely after 6 months [31]. In a case involving biliopathy, where the PVA comprised hepatic ducts, ursodeoxycholic acid was used to decrease the level of conjugated bilirubin [22].

While, in some studies, a CT scan every 12 months was the preferred monitoring strategy, most published studies indicate that sonography is the preferred imaging technique for monitoring PVA growth, as it is relatively inexpensive and does not involve radiation exposure [32].

Open surgery approach

If the PVA is growing and constricting adjacent organs, thrombosis occurs. Open surgery methods should therefore be considered in order to prevent potential rupture. An aneurysmectomy for fusiform aneurysms (aneurysm resection, followed by insertion of a synthetic or cadaveric graft as a replacement conduit) and an aneurysmorrhaphy for saccular aneurysms (normalizing the diameter of the portal vein

Deleted: Because …rder to prevent the PVA from f growing a, aimi…g… ato pre…oident…thrombosis or a rupture, an aneurysmectomy of the PVA was perfd…rmn ...

Deleted: D…agnostic role of endoscopic ultrasound (EUS) was highlighted in the …ongenital PVAs at the level of the splenomesenteric confluence. EUS confirmed the presence of of anechoic lesions adjacent to the neck of the pancreas [29]. EUS as a diagnostic tool was also used forin ...

Deleted: was used …f…r…identifying…an adjacent PVA as thea…cause of a common hepatic duct stricture, showing a lobulated hypoechoic mass, ...

Deleted: ¶

Deleted: ¶
D…se t…f i…heirs…rarity, the natural history of PVAs remains unclear, and the optimal strategy for its …anagement is controversial. FollowingAfter…ultimate …iagnosis of a PVA, treatment will depending…onf ...

Deleted: , …s it is …n 30% of cases), it does not require any active treatment, and monsurve…torilla…gce…(a,…policy of "wait and see") should be adopted [1]. While asymptomatic aneurysms smallerss…than 30 mm can be clinically observed, surgical intervention may be necessary in large asymptomatic aneurysms (>30 mm) [10]. The oO…igin, morphology and,…symptomatology of a PVA, along withd…comorbidities reg…nr…s…the …onservative treatment, are showned ...

Deleted: Fo… tr… a…here isng…thrombosis due tof…a PVA, anticoagulation treatment should be considered. In aA…recently published case, a 10- …ear- …ld boy with the PVA thrombosis of PVA,…was treated withby…enoxaparin. withby…enoxaparin. The,…thrombosis disappeared completely after 6 months [31]. In aA…case w…nvolvingth…biliopathy, where the PVA comprism…ds…hepatic ducts, ursodeoxycholic acid …as used tf…r…decreaseing ...

Deleted: surve…torilla…gce…strategy, the maj…sri…y…of …ublished studies indicateagree w…i…hat sonography be…sng…the preferred imaging technique for surveillance and …onitoring of ...

Deleted: ¶

Deleted: ¶ ...

if the remaining venous wall is of good quality) are considered for symptomatic aneurysms and to prevent a negative PVA prognosis.

The origin, morphology, PVA symptomatology and comorbidities as regards invasive treatment are shown in *Table 2*.

Fleming at al. demonstrated the efficacy of open surgery (aneurysmectomy) in three cases (two patients with an autograft and one with ePTFE), and anti-aggregation/anticoagulants were considered. The two women with an autogenous graft remained asymptomatic at 85 and 65 months, respectively; the third woman with ePTFE got thrombosis during pregnancy. The same report also included an aneurysmorrhaphy as the chosen treatment in one woman with a PVA [33].

Kim et al. presented a case with a PVA at the level of the main trunk, growing and with thrombosis complications. An aneurysm excision with an interposition bypass was successfully performed. The patient's postoperative recovery was rapid and uneventful, with normal portal flow revealed by colour Doppler ultrasonography and a contrast-enhanced CT scan [34].

Khan et al. presented a case where splenomegaly, a giant splenic artery aneurysm and a PVA were found to coexist. The patient underwent a splenectomy and excision of the splenic artery aneurysm. It was determined that her PVA shrank considerably [16]. Das et al. presented a case with thalassaemia major, splenomegaly and a PVA. After a splenectomy (necessitated by the existence of hypersplenism), the PVA significantly reduced [15].

Chadha at al. reported the case of a 66-year-old male with an acquired SV aneurysm and described novel use of a "*Sundt external carotid endarterectomy shunt*" as a temporary portacaval shunt to control portomesenteric hypertension, before transplantation of the liver [35]. A giant SV aneurysm 98 mm in size developed as a consequence of a splenectomy, an arteriovenous fistula and portal hypertension; this aneurysm was treated successfully with open surgery [36].

Male and female patients, both of whom had a congenital PVA and subsequent thrombosis complications, were treated with a hybrid operative repair involving a transhepatic catheter thrombectomy, and their aneurysms were operated on in open surgery [25, 37].

The limited number of PVAs that have been reported means that there are no clear indications for open surgery on PVAs. Koc at al. [10] studied the size of PVAs and concluded that aneurysms larger than 30 mm should be surgically treated with the aim of preventing thrombosis or rupture. On the other hand, a recently reported case of a patient with a congenital PVA 35 mm in size, with subsequent thrombosis complications, showed spontaneous resolution after 10 years [5].

Sura et al. reported the case of an 80-year-old man who had open surgery on a 37-mm PVA at the level of the main trunk [38]. The reasons for PVA surgery were not postulated, but given the congenital origin,

Deleted: , …f the remaining venous wall is of good quality) are considered for symptomatic aneurysms and to prevent a negative PVA prognosis of PVA …

Deleted: O…igin, morphology, PVA symptomatology of PVA …nd comorbidities as regards the …nvasive treatment are showned …

Deleted: …f the …pen surgery (aneurysmectomy) in three cases (two patients with an2…autograft,…and one with 1 ePTFE), asubseque…dtly…anti-aggregation/anticoagulants were considered. The two women with an autogenous graft remaineds…asymptomatic at 85 andrespectivly…65 months, respectively; the third woman with ePTFE got thrombosis during the …regnancy. The same report was …lso included an aneurysmorrhaphy as thea…chosic…n of …

Deleted: with …rowing and with complication of thrombosis complications. AHence, a… aneurysm excision with an interposition bypass was successfully performed. The patiH…nt'sr…postoperative recovery was rapid and uneventful, with normal portal flow revealed byon…colour Doppler ultrasonography and a contrast- …

Deleted: Sh…nt underwent a splenectomy and excision of the splenic artery aneurysm. It was dH…termined that her PVA,…had …hrau…ken…consideremark…bly in size [16]. Das et al. presented a case with thalassaemia major, splenomegaly and a PVA. After a splenectomy (ndu…cessita ted by the existence of hypersplenism), the PVA was …

Deleted: in …6- …ear- …ld male with an acquired SV aneurysm and described the …ovel use of a "*Sundt external carotid endarterectomy shunt*" as a temporary portacaval shunt to control portomesenteric hypertension, before transplantation of the liver [35]. A giant SV aneurysm in size 98 mm in size,… …

Deleted: of them …it…om had a congenital PVA and subsequefollowi…tg…thrombosw…sth…complications, of the thrombosis …ere treated with a hybrid operative repairment…conta…nvolving as…transhepatic catheter thrombectomy, and their aneurysms for themselves …ere s…plv…rated on w…nth…open surgery …

Commented [NK5]: The authors may want to say ...as to the efficacy of...

Deleted: aking into consid…r…lat…on s…itall report…d number of PVAs that have been reported means that,…there is …rbs… nce …f …

Deleted: f…PVAs. Koc at al. [10] sturegar…ied the size of PVAs and,…conclusi…er…d that aneurysms larger than 30 mm should be surgicaller… treated with the aiming…t…f preventing thrombosis or rupture. On the other hansi…e… a recently reported case of a patient with a congenital PVA in size …5 mm in size, follo…ith subsequentd…thrombosisy…complication of thrombo…,is …

Deleted: i… 80- …ear- …ld man whperf…r…hame… open surgery …n af…37- …m PVA at the level of the main trunk [38]. ThCl…ar…reasons for PVAopen…surgery werof PVA hav… not been …ostulated, but yet;…given this case regards the congenital origin, …

advanced age of the patient and absence of symptoms or thrombosis, it is our view that surgery was not the best treatment choice.

Interventional radiology procedures

In cases where a PVA is a consequence of portal hypertension and/or coexists with life-threatening conditions (injuries), the high risk associated with open surgery methods means that interventional radiology procedures via a percutaneous approach, endovascular approach or, better still, an endoscopic approach should be considered [1, 2].

Percutaneous approach

Shukla et al. successfully demonstrated percutaneous embolization of a saccular intrahepatic PVA and occlusion of the aneurysm, which prevented further growth or other clinical sequelae [39]. Shrivastava et al. presented the largest intrahepatic PVA and the first case where the endovascular technique was used for treatment of the same. Under sonography and fluoroscopy guidance, the PVA was directly punctured with an 18G needle and embolized with a Lipiodol-Glue combination [27].

Juscafresa et al. reported the case of an elderly female treated for an acquired SV aneurysm 45 mm in size, through a transhepatic percutaneous approach, using a VIABAHN covered stent [40]. Marmor et al. presented the case of a patient with a congenital SV aneurysm 40 mm in size. Because the aneurysm was getting larger, it was treated with an expandable stent via a transhepatic approach [41].

In one case, after liver transplantation necessitated by HCV cirrhosis, the patient subsequently developed an arterioportal fistula with an intrahepatic PVA. The first step of the treatment was transarterial embolization, and the second step was stent graft exclusion of the PVA. As there was leakage, the patient underwent liver re-transplantation [42]. Oguslu et al. demonstrated two techniques for treatment of an arterioportal fistula with a giant saccular PVA at the level of the left branch. After failure of an endovascular approach due to tortuosity and angulation of the celiac artery, access to the hepatic artery was obtained directly via a percutaneous transhepatic route, and the fistula site was embolized with an Amplatzer Vascular Plug II and coils [43].

Our review covered three patients (all males) with a PV pseudoaneurysm, all of which were a consequence of abdominal trauma or injury. In a patient with a traumatic pseudoaneurysm at the level of the splenomesenteric confluence, Ierardi et al. demonstrated a novel management strategy with a percutaneous transhepatic self-expanding stent graft [69].

A patient with a PV pseudoaneurysm at the level of the main trunk, resulting from invasive medical procedures (e.g., a percutaneous biopsy or endoscopic retrograde cholangiopancreatography (ERCP)) to address lymphomatosus infiltration of the pancreatic head (with symptoms of haemobilia), was treated, using percutaneous transhepatic covered stenting [70].

Deleted: , …d absence of symptoms and n…r thrombosis of PVA… it is from …ur point of …iew that surgery was not the best treatment of …

Deleted: ¶

Deleted: ¶ …

Deleted: ¶
¶
¶

Deleted: ¶ …

Deleted: i… eo…derly female treated for an acquired SV aneurysm 45 mm in size, through a transhepatic pP…rcutaneous approach, using a VIABAHNiabahn…covered stent [40]. Marmor et al. presented the case of a patient with a congenital SV aneurysm 40 mm in size. B, b…cause theof…growing …neurysm was getting larger, it was treated with a balloo …

Deleted: du…cessita …ed byo…HCV cirrhosis, the patient subsequently developed an arterioportal …istula with an intrahepatic PVA. The first step of the treatmei…tg…was transarterial embolizs…tion, and the second step was stent graft exclusion of the PVA. As Due …here waso…leakage, ing …he patient was …nderg…eo…t e …iver re-transplantation [42]. Oguslu et al. demonstrated two techniques o…or treatmei…tg…of an arterioportal fistula with a giant saccular PVA at the level of the left branch. After failureing …

Deleted: t…ichem…were a consequences…ofby …

Deleted: by…invasive medical procedures (e.g., such… us…percutaneous biopsy or endoscopic retrograde cholangiopancreatography (ERCP)) to addru…ss to lymphomatosus infiltration of the pancreatic head (…ith symptoms of haemobilia), was treateding…usingby …

In the last case, involving a patient with a pseudoaneurysm of the portal venous system resulting from a motor vehicle collision, the patient was brought into the emergency department with diffuse abdominal pain and bowel shock. Unfortunately, the patient soon succumbed to his injuries [71].

Endovascular approach

Gaining access to the treatment zone can be challenging, and the target vessel may have tortuosity and elongation due to haemodynamic changes created by the hyperdynamic flow. Kimura et al. presented a case involving a hepatectomy (hepatocellular carcinoma), where the patient subsequently developed an arterioportal fistula with hepatofugal flow and a 40-mm-diameter PVA. After selective embolization of the anterior hepatic artery, the PVA disappeared, and portal flow was normalized [44].

An endovascular approach includes creation of a transjugular intrahepatic portosystemic shunt (TIPS). In patients with portal hypertension, an attempt may be made to decrease portal venous pressure in order to reduce the size of the aneurysm. Our review covered four patients with a PVA where the treatment of choice was a TIPS. Tsauo et al. presented a case involving a PVA resulting from portal hypertension associated with Budd-Chiari syndrome. For the first time, a TIPS was created without complications. The patient's abdominal pain completely ceased within two days, and she remained asymptomatic during the one-year follow-up [14]. Ding et al. presented a case with a PVA at the level of bifurcation, with comorbidities such as portal hypertension, liver cirrhosis and HBV chronica. A TIPS successfully decreased the patient's portal hypertension and reduced the size of the PVA from 53 x 76 mm to 23 x 25 mm. Two years later, a CT scan and digital subtraction angiography revealed that the aneurysm had disappeared. The patient remained asymptomatic for 72 months [45]. Dunlap et al. also used a TIPS successfully to treat a PVA resulting from portal hypertension and liver cirrhosis [46]. Kohlbrenner et al. demonstrated transhepatic pharmacomechanical thrombolysis of a large thrombosed PVA. This was followed by insertion of a TIPS, along with an additional trans-TIPS thrombectomy to improve sluggish portal outflow and prevent re-thrombosis. Nine months later, an MRI showed complete resolution of the thromb[47].

Endoscopic approach via ERCP

In older patients with a PVA and biliopathy and jaundice complications, ERCP with biliary stenting can be an appropriate treatment choice. In an 80-year-old male with liver cirrhosis and portal hypertension, an acquired PVA at the level of the left branch was found. The patient had developed biliopathy due to compression of the common bile duct; this complication was successfully treated endoscopically via ERCP with a biliary stent [23]. Sun et al. reported the case of an 85-year-old man with cholangitis complications from PVA-induced compression. Given the age of the patient, surgery was not considered, and instead an ERCP biliary stent was deployed several times [24].

Conclusion

Deleted: ed…from aby…motor vehicle collision, the patient was brought into the emergency department wexp…thried…diffuse abdominal pain andue to…bowel shock bowl ...

Deleted: ¶

Deleted: To re…ccess toh…the treatment zone can be a challenging issue… and the target vessel may have tortuosity and elongation due to haemodynamic changes created by the hyperdynamic flow. Kimura et al. presented a case w…nvolving ath…hepatectomy (hepatocellular carcinoma), where the patient subsequently developed an arterioportal fistula with hepatofugal flow and a 40- …m- in …iameter PVA. After selective embolizs…tion of the anterior hepatic artery, the PVA diss…ppeared, and portal flow was normal ...

Deleted: E…dovascular approach includes creation of a transjugular intrahepatic portosystemic shunt (TIPS). In patients with portal hypertension, an attempt may be made to decrease …ortal venous pressures…in ordan att…rmpt…to dec…educas… the size of the aneurysm. Our review covered four patients with a PVA where the treatment of choice was a TIPS. Tsauo et al. presented a case w…nvolving ath…PVA ras a co…n…ultieque…gce…o…rom portal hypertension asin the …ocett…ated withng of…Budd- …hiari F, f…r the first time, a TIPS was created without complications. TS…e had com…ale…ie resolutio… of …'s abdominal pain completely ceased within two2…days, and she remained asymptomatic duafte…ing the one1… …ear of follow-up [14]. Ding et al. presented a case with a PVA at the the level of bifurcation, withere were ...

Formatted ...

Deleted: f…er, a CT scan and digital subtraction angiography revealed that the aneurysm had disappeared. The patient has …emained asymptomatic for 72 months [45]. Dunlap et al. alsothird time…used a TIPS successfully tf…r…the …reat ament of…PVA reas a con…ultieque…gce…o…rom portal hypertension and liver cirrhosis [46]. Kohlbrenner et al. demonstrated transhepatic pharmacomechanical thrombolysis of a large thrombosed PVA. T, t…is was followed by insertion of a TIPS, along placement … ...

Commented [NK6]: The authors may want to say ...thrombus...

Deleted: ¶

Deleted: complication of …iliopathy and jaundice complications, ERCP with biliary stenting canould…be an appr meth…priated of…treatment choice. In an 80- …ear-old male,…with liver cirrhosis and portal hypertension, an acquired PVA at the level of the left branch was found. The patient had developed biliopathy dD…e to the …ompression ofn…the common bile duct there was a biliopathy… this complication wasof PVA…successfully was …reated endoscopically via ERCP with a biliary stent [23]. Sun et al. reported the case of ai… 85- …ear- …ld man reported wcompl…ca…hion of…cholangitis complications fromby…PVA-induced compression. GivDu…n to …he age of the patient, surgery was not considered, vi…nd instead ...

Deleted: ¶

PVAs are rare morphological abnormalities of the portal venous system, accounting for 3% of all venous aneurysms in the human body. The number of reported PVAs across the world now stands at about 280: the 200 PVAs covered in the previous review published in 2015 [1], the 18 cases in the retrospective study [2] and the 62 PVAs in our review covering the last seven years. PVAs can be congenital or acquired, located mainly at the level of confluence, main trunk, branches and bifurcation. Up to 30% of patients can be asymptomatic, and non-specific abdominal pain should be investigated to exclude other pathological causes, such as cholecystitis or peptic ulcer disease, etc.

Thrombosis complications occur in approximately 19–23% of patients, and biliopathy occurs in approximately 4–6% of patients. Other complications can also arise from compression due to a PVA, including thrombosis of the ICV and intestinal obstruction. Diagnosis of a PVA is based on spectral and colour Doppler sonography, and CT and MRI imaging. EUS and IDU have also been used as a diagnostic tool.

If a PVA is asymptomatic, it does not require any active treatment, and monitoring (a policy of "wait and see") should be adopted. The first choice for treatment of PVA thrombosis is anticoagulation medication. If the PVA is getting larger and compressing adjacent organs, thrombosis will occur, so to prevent a potential rupture, open surgery methods such as an aneurysmectomy or an aneurysmorrhaphy should be considered. Given the risk associated with open surgery methods, interventional radiology procedures via a percutaneous approach, endovascular approach or, better still, an endoscopic approach should be considered for cases where a PVA is a consequence of portal hypertension and/or coexists with life-threatening conditions (injuries).

Deleted: …VA i… are rare morphological abnormalitiesy…of the portal venous system, with prev…len…counting fore …3% of all venous aneurysms in the human body. ThR…gards …

Deleted:

Deleted: of …VAs covered in the previous review published in 2015 [1], the 18 cases of PVA …n the retrospective study [2],…and the 62 PVAs have b…ee… c…vered by o…r review covering the last seven years, prevalence of reported PVA in the world up to now counts about 280… PVAs canould…be congenital or acquired, located mainly at the level of confluence, main trunk, branches and bifurcation. Up to 30% of patients can beis…asymptomatic, and non-specific abdominal pain should be clar…nvestf…gated to excludeing…other pathological causentit…,y…such as cholecystitis or, …

Deleted: C…mplication of thrombosi… occurs…in approximately in …9–…3% of patients, . Complicat…io…d of…biliopathy occurs in approximately in …—…% of patients. Other complications caorigi… also arise from by compression due tof…a PVA, including thrombosis of the ICV,…and intestinal obstruction. Diagnosis of a PVA is gradually …ased on the …pectral and colour Doppler sonography, and CT and MRI imaging. , in the last time …

Deleted: surve…torilla…g (a ce, …olicy of "wait and see") should be adopted. The fF…rst choice for treatment of PVA choice for the …hrombosis of PVA…is the …nticoagulation medication. If thsiz… of …VA is gettrow…ng,…larger h…nds…compressingnificant touch with…adjacent organs, thrombosis will occurs… soaiming…to prevent a potential rupture, open surgery methods such as an aneurysmectomy or and…aneurysmorrhaphy should be considered. Given the risk associated with open surgery methods, interventional radiology procedures via a percutaneous approach, endovascular approach or, better still, an endoscopic approach should be considered for In …ases where is … PVA is a consequence of the …ortal hypertension and … …r coexists with the …ife-thr dang…ateningrous…conditions (injuries), due to high risk for the open surgery methods, interventional radiology procedures via percutaneous approach, endovascular approach and even more endoscopic approach should be considered …

Date: December 20, 2022

Non-Native Speakers of English Editing Certificate for "*World Journal of Clinical Cases*"

I, MSc. MD Admir Kurtcehajic the first and corresponding author of the Review article

titled "**Portal Vein Aneurysm – etiology, multimodal imaging and current management**",

declare that the authors of the present manuscript are non-native English speakers.

Our first version of the manuscript was proofread by the professional agency:
https://www.englishproofread.com/

Our second (revised version) of the manuscript has been reviewed for clarity by a native

English speaker with academic English degree - Sanela Coldwell.

Sanela Coldwell Sanela Coldwell

Country of origin and full address: United Kingdom, 13 Netley Road, Morden, Surrey, SM4 6JP

Telephone: +44 07736 28 2870

Mail: Sanela coldwell@yahoo.com

Best Regards.
Admir Kurtcehajic