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A systematic review and meta-analysis: prevalence and clinical implications of anatomical variants of the hepatic portal vein

Juan José Valenzuela-Fuenzalida[1,4,6], Benjamín Rodríguez-Osorio[1,6], Cristian Salgado-Torres[1,6], Pablo Nova-Baeza[1,6], Mathias Orellana-Donoso[2,6], Alejandro Bruna-Mejías[3,6], Roberto Avila-Sepulveda[1,6], Álvaro Becerra-Farfán[4,6], Macarena Rodríguez-Luengo[1,6], Juan Sanchis-Gimeno[5,6], Guinevere Granite[6,7] & Héctor Gutiérrez-Espinoza[6,8]✉

The hepatic portal vein is the main vascular route responsible for collecting blood from the liver, spleen, pancreas, stomach, gallbladder, and intestines. Its key function is to metabolize the components acquired from the blood. The objective of this study was to analyze the characteristics of HPV variants and understand the possible clinical considerations that arise with them. The databases Medline, Scopus, Web of Science, Google Scholar, Cumulative Index to Nursing and Allied Health Literature and Latin American and Caribbean Literature in Health Sciences were researched until January 2024. Tree authors independently performed the search, study selection and data extraction. Methodological quality was evaluated with an assurance tool for anatomical studies. Pooled prevalence was estimated using a random effects model. A total of 31 studies met the established selection criteria. In this study, 21 articles were included for the meta-analysis with a total of 51,244 subjects. Of these 21 articles, the topics studied came mainly from Europe and Asia, with three (n = 554; 1.08%) and 11 articles (n = 50,090; 97.75%) respectively, also having six articles from North America (n = 442; 0.86%) and one from Africa (n = 158; 0.31%), discarding the articles from Oceania and South America. For the HPV trifurcation variant, it was 8% (CI = 7-10%). Apropos the right posterior portal vein variant, as the primary tributary from the main HPV, it was 7% (CI = 4-11%). About the right anterior portal vein variant originating from the left portal vein, it was 4% (CI = 1-6%). Finally, the prevalence of the isolated variants was 2% (CI = 1-3%). The knowledge of HPV and its anatomical variants is of utmost importance for both medical professionals and anatomists, as it is one of the vessels that collects blood from many important viscera found in the abdominal cavity, any structural alteration could be crucial in diagnosis and surgical procedures.

Keywords Portal vein, Hepatic portal vein, Variation portal vein, Portal triad, Variation anatomical, Clinical anatomy

[1]Departamento de Morfología, Facultad de Medicina, Universidad Andrés Bello, Santiago 8370146, Chile. [2]Escuela de Medicina, Universidad Finis Terrae, Santiago 7501015, Chile. [3]Departamento de Ciencias y Geografía, Facultad de Ciencias Naturales y Exactas, Universidad de Playa Ancha, Valparaíso 2360072, Chile. [4]Departamento de Ciencias Química y Biológicas, Facultad de Ciencias de la Salud, Universidad Bernardo O'Higgins, Santiago 8370993, Chile. [5]GIAVAL Research Group, Department of Anatomy and Human Embryology, Faculty of Medicine, University of Valencia, Valencia 46001, Spain. [6]Faculty of Health and Social Sciences, Universidad de Las Américas, Santiago 8370040, Chile. [7]Department of Surgery, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA. [8]One Health Research Group, Universidad de las Americas, 170124 Quito, Ecuador. ✉email: hector.gutierrez@udla.edu.ec

Anatomy and function of the HPV

The hepatic portal vein (HPV) system constitutes the principal vascular route for directing blood to the liver, primarily from the spleen, pancreas, stomach, gallbladder, and intestines. Its key function is the transportation of nutrient-rich blood from various organs to the liver, where metabolism occurs. Subsequently, this blood is redirected into the systemic circulation via the hepatic veins, ultimately draining into the inferior vena cava (IVC). Structurally, the HPV system is established by the confluence of two major veins: the splenic vein (SV), stemming from the spleen, and the superior mesenteric vein (SMV), which handles drainage from the small intestine, caecum, ascending and transverse parts of the colon, and distal parts of the stomach and greater omentum. It is important to note that the inferior mesenteric vein (IMV) usually drains into the SV. This conventional arrangement is a commonly reported structure in the studies analyzed. The convergence of these veins results in the formation of the HPV, approximately 7–8 cm in length, which is responsible for delivering roughly 75% of the liver's blood supply. The remaining portion of hepatic blood flow is supplied by the common hepatic artery (CHA)[1].

The HPV typically resides posterior to the pancreatic neck and slightly to the left of the descending duodenum, ascending within the hepato-duodenal ligament; a component of the lesser omentum. It lies posterior to the proper hepatic artery (PHA) and the common bile duct (CBD). Together, these three structures constitute the portal triad, leading toward the hepatic hilum. Upon entering the liver, the HPV is divided into two primary tributaries: the left portal vein (LPV), serving hepatic segments I, II, III, and IV, and the right portal vein (RPV). The latter further divides into the right anterior portal vein (RAPV), supplying segments V and VIII, and the right posterior portal vein (RPPV), catering to segments VI and VII. This anatomical distribution is predominant, occurring in approximately 65–80% of individuals[2].

Anatomical variations of the HPV

Variations from this common anatomical arrangement range from differences in the HPV's location and formation to divergences in its primary tributaries. The most frequently observed variant is the trifurcation of the HPV, present in about 8–10% of the population[3]. The prevalence of other variations is less consistently reported across different studies; hence, a specific percentage of occurrence is challenging to ascertain. Currently, there is no uniform classification for all variants; however, the trifurcation of the HPV is generally categorized as type II. The emergence of the RPPV as the primary tributary from the main HPV characterizes the type III variant. The occurrence where the RAPV originates from the LPV is referred to as type IV, while the common bifurcation pattern is identified as type I, a classification proposed by Lee (2008)[7].

Embryonic development of the HPV

The embryonic development of the HPV system occurs between the 4th and 12th weeks of gestation. It originates from two yolk (omphalomesenteric) veins, which are integral in draining blood from the yolk sac toward the heart. These veins undergo anastomosis around the duodenum. Through selective regression of the paraduodenal anastomoses, a singular vessel, known as the portal trunk, is formed. Variations in the hepatic portal system often arise from alterations in the involution of these anastomoses[4].

Clinical relevance

For patients undergoing liver and biliary surgeries, as well as liver transplants, considering these variations is critical. This insight is crucial for planning and conducting surgical operations with increased safety and efficacy. Moreover, such knowledge becomes particularly vital during invasive procedures like HPV embolization or portosystemic shunt operations, commonly performed in scenarios of venous hypertension. These procedures typically involve creating connections between the right hepatic vein and the RPV, thereby necessitating an in-depth analysis of the anatomical variances present[5].

Regarding the knowledge gap that we seek to resolve in this review, it is to know how HPV variants occur in the world population through the knowledge collected in previous studies, resolving concerns such as the specific description of HPV variants. How these are associated with pathological alterations of the liver or surgical procedures of this same organ. In relation to the above, we have not found systematic review type literature that makes the aforementioned relationship. Given the aforementioned points, the following research questions arise: What types of HPV variants can occur? What is the prevalence of these variants? Do they have any clinical significance when performing hepatic surgical procedures or addressing other types of pathologies? These questions are sought to be answered in this study.

The objectives of this systematic review and meta-analysis were to analyze the characteristics of the main anatomical variants associated with the HPV described in the literature to understand the clinical correlation between the presence of HPV variants and various surgical and diagnostic procedures, and to establish a more precise description of the HPV anatomy, all based on the best available scientific evidence in the literature.

Methods

Protocol and registration

This systematic review and meta-analysis were conducted and reported in according with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The registration number in the International Prospective Register of Systematic Reviews (PROSPERO) is CRD42022227061.

Eligibility criteria

Studies on the presence of HPV variants and their association with any clinical condition were considered eligible for inclusion if the following criteria were met: (1) population: sample of dissections or images of the

HPV; (2) outcomes: HPV prevalence, variants, and their correlation with pathologies of the abdominal supra-mesocolic and infra-mesocolic region. Additionally, anatomical variants were classified and described based on normal anatomy and classifications proposed in the literature; (3) studies: This systematic review included research articles, research reports, and original research published in English in peer-reviewed journals indexed in some databases used to collect the studies. Conversely, the exclusion criteria were as follows: (1) population: animal studies; (2) studies that conducted analysis of variants in the other hepatic vein region; (3) studies: letters to the editor or comments.

Electronic search

We systematically searched MEDLINE (via PubMed), Web of Science, Google Scholar, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, and the Latin American and the Caribbean Literature in Health Sciences (LILACS) from inception until January 2024. The search strategy included a combination of the following terms: "Portal Vein" (Mesh), "Hepatic portal vein" (No Mesh), "Variation portal vein" (No Mesh), "Portal triad" (No Mesh), "Variation anatomical" (No Mesh), and "Clinical anatomy" (No Mesh), using the Boolean connectors: AND, OR, and NOT. If we extrapolate data to the combination of Boolean connectors, for the PICO strategy, patients: Subjects with hepatic approach or cadavers approached in the supra-mesocolic region; Intervention: subjects with HPV variants; Comparison: subjects without HPV variant; Outcomes: cadaveric and imaging findings consistent with the presence of the anatomical variant. The search strategies for each database are available in the supplementary material (Supplementary Table S1).

Study selection

To safeguard the reliability of the included and excluded studies, two authors independently (BR and CS) examined the titles of the studies that met the search criteria in the different databases, after there were studies with a coincidence in the choice, for which only one of the authors was chosen, a discussion was held and a consensus was reached to include or exclude the studies, after that the same method was repeated but now with the summaries recovered from the searches by qualification. Finally, the full text of the studies that the authors considered potentially relevant was obtained. A third reviewer (PN) was involved if consensus could not be reached to exclude or include studies.

Data collection process

Two authors (JV and MO) independently extracted data on the outcomes of each study. The following data were extracted from the original reports: (I) authors and year of publication, (II) country, (III) type of study, (IV) sample characteristics (sample size, age, distribution, and sex), (V) prevalence and morphological characteristics of HPV, (VI) statistical data reported by each study, and (VII) main results.

Assessment of the methodological quality of the included studies

The quality assessment was carried out using the Anatomical Quality Assurance (AQUA) tool for anatomical studies, proposed by the International Evidence-Based Anatomy Working Group (IEBA)[6]. Data extraction and quality assessment were independently conducted by two reviewers (JJV and JM). The agreement rate between the reviewers was calculated using kappa statistics. To eliminate detection bias, a third reviewer (HG-E, with higher academic degree and more experience in scientific writing) analyzed the data from each selected study for a double-blind analysis to reach a consensus that could eliminate study selection results. For the representation of kappa index data, the following standards were used: 0 poor, 0.01–0.20 mild, 0.21–0.40 average, 0.41–0.60 moderate, 0.61–0.80 substantial, and 0.81–1 almost perfect.

Publication bias

A funnel plot was created using JAMOVI to assess publication bias. The funnel plot graph shows the data that most affects this criterion, with includes the statistical significance of the primary article and its sample size. This graph plots sample measurement against the exposure association or confidence interval transformed into standard error, against the sample size.

Statistical methods

The data extracted from the meta-analysis was interpreted by calculating the prevalence of the HPV variants using JAMOVI software. The DerSimonian-Laird model with a Freeman-Tukey double arcsine transformation was used to combine the summary data. Additionally, a random effects model was utilized due to the high heterogeneity in HPV prevalence data among included studies. The degree of heterogeneity was assessed using the chi^2 test and the heterogeneity (I^2) statistic. For the chi^2 test, a P value of 0,10 was considered significant as proposed by the Cochrane collaboration. Values of the I^2 statistic were interpreted with a 95% confidence interval [CI] in the following manner: 0–40% might not be important, 30–60% might indicate moderate heterogeneity, 50–90% might represent substantial heterogeneity, and 75–100% could indicated a significant amount of heterogeneity[6].

Results

Selection of articles

The search process yielded a total of 31 articles from various databases, aligning with the criteria and search terms established by our research team. A filtration process was applied, focusing on the titles and/or abstracts of these articles. Out of the initial pool, 21 articles were selected for inclusion in the meta-analysis. These articles were chosen based on their comprehensive study of the sample, detailed statistical data for each variant, and their utilization of a clear methodology.

Conversely, eight articles, primarily consisting of clinical case reports, were excluded from the meta-analysis. These reports, while offering valuable clinical and anatomical insights, primarily detailed individual cases and thus lacked the broader statistical foundation required for substantive analysis of the variables. However, these case reports were still considered valuable for the clinical and anatomical aspects of this study. The kappa index for the selection of these studies was 0.79, indicating that it is substantial.

The total sample size encompassed 54,588 individuals. For the purposes of the meta-analysis, 51,244 participants, derived from the 21 selected articles, were included. This sample comprised patients, imaging studies, and cadaveric specimens (Fig. 1).

Characteristics of the studies and the study population

Our review of 31 studies revealed a diverse geographical distribution, reflecting a global perspective on the research topic. In South America, one study was identified, while North America contributed six studies, with the majority originating from Canada and the United States. Asia was significantly represented, contributing 14 studies and demonstrating considerable geographic diversity, especially with a notable representation of the Chinese population. Remarkably, none of the studies originated from Oceania. In Europe, nine articles were included, exhibiting a broad range of geographical variance. Additionally, the collection of research included one study from Africa, further enhancing the global scope of our review.

Out of the 21 articles selected for the meta-analysis, which encompassed a total of 51,244 individuals. For the region of the studies, the geographical region reported in the study methods was added. If this was not reported, the affiliation of the authors was taken. Only 1 study reported affiliation in more than one country of its authors, therefore which was written to the authors where the study was carried out, giving the information and being able to eliminate this region bias in the included studies The majority of the studies were from Europe and Asia, with three articles ($n = 554$, accounting for 1.08% of the sample) and 11 articles ($n = 50,090$, representing 97.75% of the sample), respectively. Moreover, the research comprised six studies from North America ($n = 442$, 0.86% of the sample) and one study from Africa ($n = 158$, 0.31% of the sample). It is noteworthy that while one study originated from South America, none of the studies included in the meta-analysis were from Oceania or South America (Fig. 2).

The gender distribution within our comprehensive pool of 54,588 participants showed a varied pattern. Of these, 2645 were identified as male and 2434 as female. Notably, in 10 studies accounting for 49,509 participants, gender was not specified. Within the subgroup of 51,244 individuals selected for our meta-analysis, the gender distribution revealed 2147 males and 2006 females. Additionally, gender details were not specified for 47,091 individuals in nine studies of this subset, as detailed in Table 1.

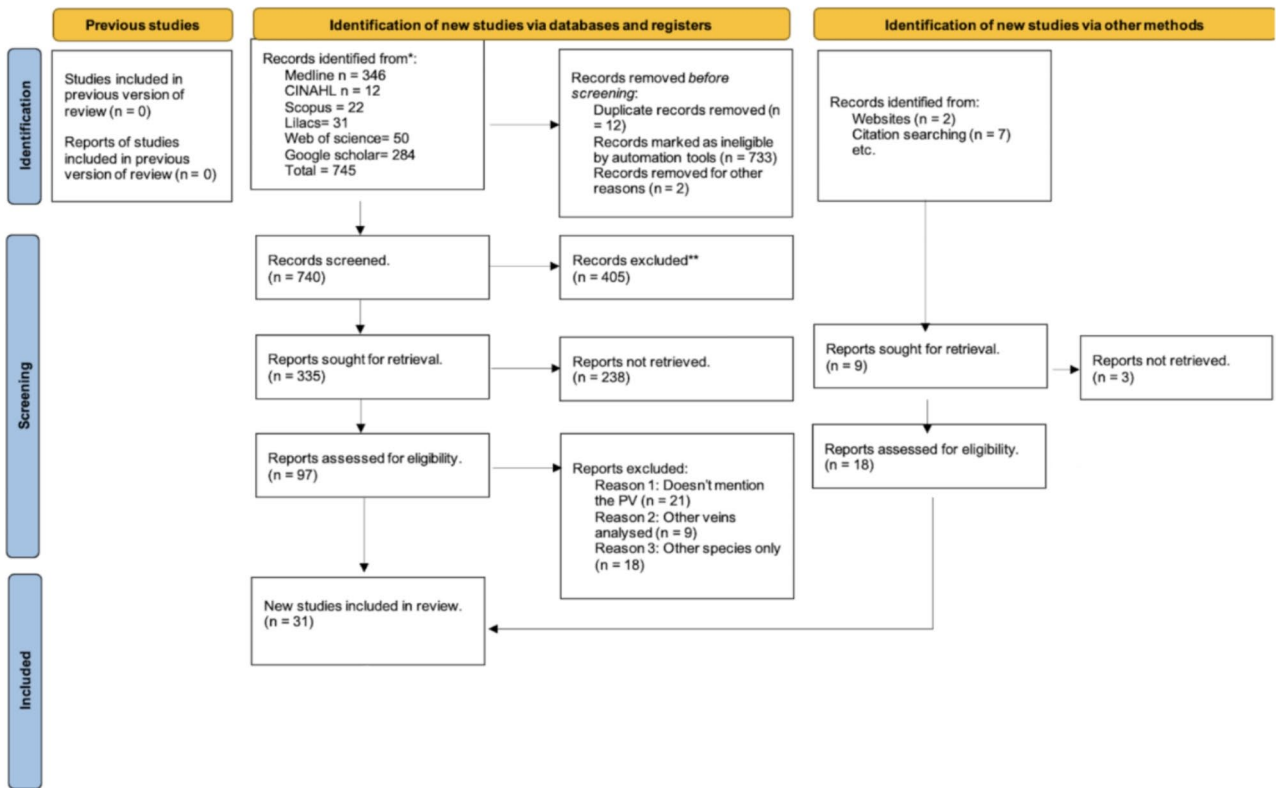

Fig. 1. Flowchart for search strategy.

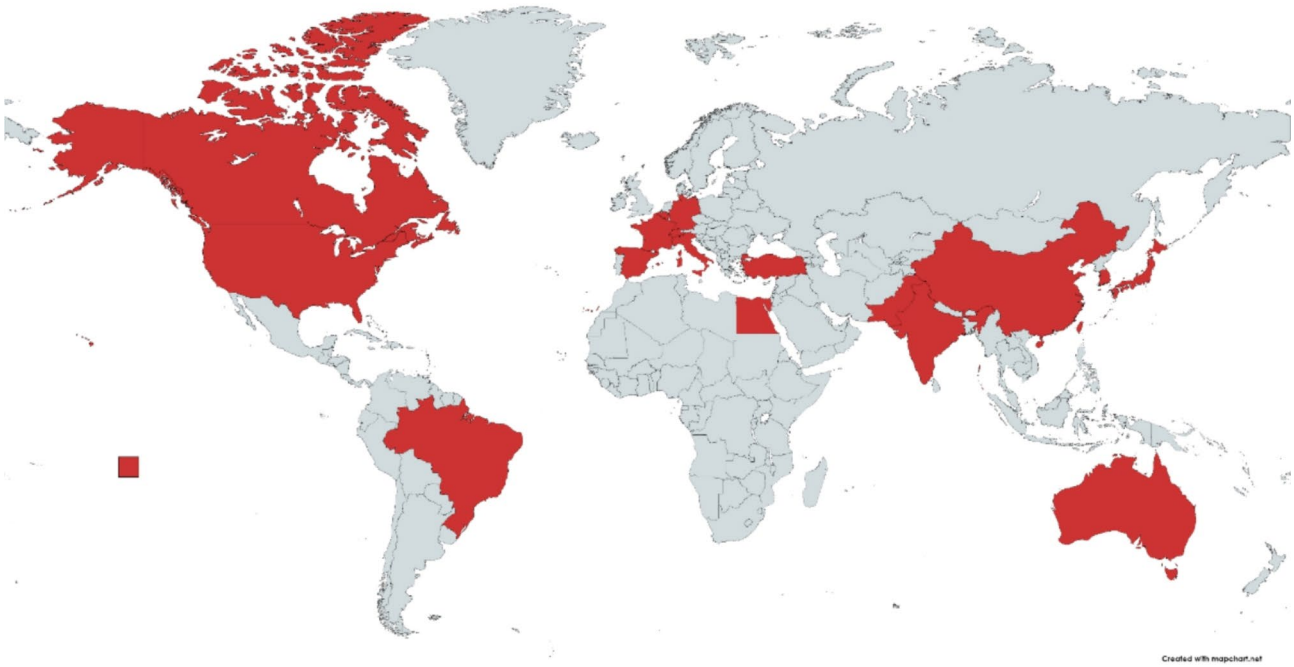

Fig. 2. Geographic distribution included articles.

Variant descriptions

In this study, various anatomical variants of the HPV system were thoroughly investigated to elucidate their complexity and potential clinical ramifications. These variants were meticulously categorized, offering an in-depth perspective on the anatomical diversity within the study population (Table 2). In this research, we mainly adopt the classification framework proposed by[7], which is widely acknowledged in the literature. This framework is centered around the tributary patterns of the HPV. The type I variant, deemed the standard configuration and most prevalent in the population, is characterized by the division of the main HPV into two primary tributaries: the LPV, supplying hepatic segments I, II, III, and IV, and the RPV. The latter further divides into the right anterior tributary, serving segments V and VIII, and the right posterior tributary, catering to segments VI and VII of the liver.

The type II variant is distinguished by the trifurcation of the HPV. This variant mirrors the normal pathway, situated posterior to the neck of the pancreas and adjacent to the descending part of the duodenum, ascending within the hepato-duodenal ligament and posterior to the PHA and the CBD. However, it differs in its early division upon entry into the hepatic hilum, where the main HPV splits into three main tributaries at a single point: the LPV tributary, the RAPV tributary, and the RPPV tributary. These tributaries distribute similarly to the standard variant, vascularizing the respective liver segments[5].

The type III variant adheres to the previously described pathway, positioned behind the neck of the pancreas and posterior to the PHA and the CBD, ascending within the hepato-duodenal ligament. However, its distinguishing feature is the early formation of tributaries of the right posterior tributary, which emerges as the first tributary of the main HPV. Subsequently, a common trunk is formed within the main HPV, catering to both the right anterior tributary and the LPV. These tributaries then follow their typical routes to supply the respective hepatic segments.

Similarly, the type IV variant follows this path but is usually characterized by an atypical origin of the right anterior tributary. Rather than emerging from the RPV, which is the customary route, it is known to initiate from the LPV. This variation alters the distribution pattern, yet the tributaries continue to vascularize their corresponding hepatic segments.

While the aforementioned variations are the predominant phenotypes within the population, less prevalent variants are also discernible. These encompass the prepancreatic post-duodenal portal vein (PPPV), which not only diverges in anatomical location but also exhibits diminished wall strength and thickness, potentially impacting its interactions with neighboring structures. Furthermore, the study also identifies several less common HPV variants: an accessory tributary of the RPV; a non-bifurcating main HPV; an RPV that does not divide; an absence of the RPV; and a direct connection of the HPV to the IVC, a condition classified by Abernethy and denominated as Abernethy syndrome[8].

In addition to variations in its tributary patterns, the HPV also exhibits differences in its formation. The standard and most prevalent form in the population arises when two veins, the SV and the SMV, merge to create the HPV. This formation is typically complemented by the drainage of the IMV into the SV. Another notable variant occurs when the IMV drains at the intersection of the SMV and the SV, resulting in the main HPV being

Author	Example and Total *N*	Prevalence	Characteristics of variants	Geographic region	Sex example	Clinical consideration
Aboueisha et al., 2013[11]	158 Subjects subjected to magnetic resonance angiography	18/158	HPV trifurcation: 16 subjects (10.1%) HPV is divided into two RPPV and a common trunk that is divided into RAPV and LPPV: 1 subject (0.63%) HPV is divided into 4 RPV and 1 LPV: 1 subject (0.63%)	Egypt	Not specified	Clinical consideration for liver donation
Akashi et al., 2023[10]	1 Subject subjected to CT	1/1	PPPV case. In the hepatic hilum the HPV is dilated, coiled and with multiple tributaries	Japan	Male: 1 Female: 0	Surgical consideration, in cases with PPPV that cause fragility and thinness in the wall of the portal vein
Anwar et al., 2020[12]	500 Subjects subjected CT angiography	24/500	Typical bifurcation of HPV: 476 subjects (95.2%) HPV trifurcation: 8 subjects (1.6%) RAPV arises of LPV: 16 subjects (3.2%)	India	Male: 301 Female: 199	Consideration for surgical procedures
Arviza et al., 2021[13]	31 Subjects (corpses) subjected to autopsy 213 subjects subjected to CT	72/244	In corpses: HPV trifurcation: 9 subjects (29%) RAPV arises of LPV: 1 subject (3.2%) In images: HPV trifurcation: 26 subjects (26.2%) RPPV first tributary of the HPV: 31 subjects (14.6%) No bifurcation of RPV: 4 subjects (1.9%) RAPV arises of LPV: 1 subject (0.5%)	Spain	Male: 119 Female: 94 31 Unspecified Subjects	Surgical consideration in liver transplants
Asad Ullah et al., 2020[14]	500 Subjects subjected to CT	62/500	Typical HPV bifurcation: 438 subjects (87.6%) HPV trifurcation: 18 subjects (3.6%) RPPV first tributary of the HPV: 22 subjects (4.4%) Separate tributary of the RPV to segment VII: 6 subjects (1.2%) Separate tributary of the RPV to segment VI: 16 subjects (3.2%)	Pakistan	Male: 256 Female: 244	Surgical consideration. Know the prevalence of variations in HPV in the population through CT to have considerations in case of possible surgeries
Bartsch et al., 2016[31]	1 Clinical case report of a subject subjected to a cholecystectomy	1/1	HPV trifurcation, with biliary variability: 1 subject (100%)	Germany	Males: 1 Female: 0	Clinical correlation between biliary and portal anatomical variations, with pancreatitis and Conradi-Hünermann-Happle syndrome
Bogetti et al., 2001[15]	17 Subjects subjected to MRI	2/17	HPV trifurcation: 2 subjects (11.7%)	USA	Not specified	Clinical consideration in liver transplantation, highlighting preoperative imaging relevance
Carr et al., 2003[16]	25 Subjects subjected to MRI angiography	6/25	HPV trifurcation: 4 subjects (16%) Early origin of HPV: 2 subjects (8%)	USA	Male: 12 Female: 13	Clinical consideration to prevent problems due to HPV variants
Chaib et al., 2005[17]	60 Livers from corpses evaluated in autopsies	10/60	HPV trifurcation: 9 subjects (15%) Absence of HPV bifurcation: 1 subjects (1.6%)	USA	Not specified	Surgical consideration in cases of liver transplants, to guarantee vascular supply. The absence of HPV bifurcation is a contraindication for a split liver transplant
Chirica et al., 2005[50]	1 subject subjected to a physical examination and CT	1/1	Situs inversus with multiple vascular variation, including the prepancreatic and preduodenal HPV	France	Male: 0 Female:1	Clinical correlation of situs inversus with vascular anatomical variants. Surgical consideration for a hepatectomy in the presence of a preduodenal portal vein
Coulier et al., 2021[32]	1 Subject undergoing a clinical review	1/1	Existence of an asymptomatic left isomerism with preduodenal portal vein	Belgium	Male: 1 Female: 0	Diagnostic consideration to relate the variant to the symptoms presented
Covey et al., 2004[18]	200 Subjects subjected to CT	70/200	Typical bifurcation of HPV: 130 subjects (65%) HPV trifurcation: 18 subjects (9%) RPPV first tributary of the HPV: 26 subjects (13%) Variation in the vascular distribution of RPV in the liver segments: 26 subjects (13%)	USA	Not specified	Clinical consideration in a percutaneous hepatobiliary intervention or in a surgical procedure
Gómez Contreras et al., 2019[33]	2 Clinical case reports	2/2	Abernethy syndrome: Connection between the IVC and RPV causing portosystemic flow	Spain	Male: 1 Female: 1	Clinical consideration in cases of encephalopathies due to portosystemic communication
Gou et al., 2022[19]	46,179 Pregnant female subjects subjected of ultrasound	8266/46,179	RPPV first tributary of the HPV: 5609 subjects (12.15%) HPV trifurcation: 2657 subjects (5.75%)	China	Not specified	Clinical consideration for monitoring fetal development
Higashihara et al., 2022[34]	1 Subject subjected to CT	1/1	PPPV case.	Japan	Male: 0 Female: 1	Surgical consideration in cases with PPPV, which results in fragile walls with difficult surgical access
Hyidar et al., 2023[35]	2 Subjects subjected to surgery	2/2	In both cases the HPV was oriented anteriorly to other structures of the portal triad.	Pakistan	Male: 1 Female:1	Surgical consideration when performing procedures in the portal triad, taking into account its variants
Kim et al., 2012[20]	104 Subjects subjected to CT	18/104	HPV trifurcation: 13 subjects (12.5%) RPPV first tributary of the HPV: 4 subjects (3.84%) RAPV arises of LPV: 1 subject (0.96%)	South Korea	Not specified	Surgical consideration in transplants, for cases of terminal liver disease. With the aim of maintaining correctly vascularized grafts
Koc et al., 2007[21]	1120 Subjects subjected to CT	242/1120	HPV trifurcation: 139 subjects (12.4%) RPPV first tributary of the HPV: 103 subjects (9.2%)	Turkey	Male: 588 Female: 532	Clinical consideration in invasive procedures
Continued						

Author	Example and Total *N*	Prevalence	Characteristics of variants	Geographic region	Sex example	Clinical consideration
Krumm et al., 2011[9]	916 Subjects subjected to CT	572/916	IMV drains at the confluence of the SV and the SMV: 264 subjects (28.8%) IMV drains into the SMV: 176 subjects (19.2%) Variations in vascular diameter: 132 subjects (14.4%)	Germany	Male: 493 Female: 423	Consideration to avoid complications in abdominal surgery
Lee et al., 2008[7]	310 Subjects subjected to liver transplants	45/310	HPV trifurcation: 22 subjects (7.1%) RPPV first tributary of the HPV: 20 subjects (6.4%) RAPV arises of LPV: 3 subjects (0.96%)	South Korea	Not specified	Surgical consideration for liver transplants, taking into account the ramifications of HPV
Lee et al., 2004[22]	108 Subjects subjected to MRI	12/108	HPV trifurcation: 4 subjects (3.7%) Other types of variants of the RPV: 7 subjects (6.48%) Accessory tributaries of RPV: 1 subjects (0.92%)	USA	Male: 48 Female: 60	Surgical consideration in cases of liver transplants, to guarantee vascular supply. Relationship between biliary anomalies and portal anomalies
Liu., 2020[30]	810 Subjects subjected to CT	455/810	Typical HPV bifurcation: 355 subjects (43.8%) HPV Trifurcation: 250 subjects (30%) Arched RPPV without tributaries: 71 subjects (8.7%) RAPV with 4 sub-tributaries: 14 subjects (1.7%) RAPV with trunks with multiple sub-tributaries: 13 subjects (1.6%) RAPV arises from LPV: 92 subjects (11.35%) tributary that supplies segment VI arises from RAPV: 15 subjects (1.85%)	China	Male: 270 Female: 540	Surgical consideration in transplants, for pre-operative plans. With the aim of maintaining correctly vascularized grafts
Macdonald et al., 2005[23]	32 Subjects subjected to CT	7/32	HPV trifurcation:6 subjects (18.75%) RAPV arises of LPV: 1 subjects (3.1%)	Canada	Not specified	Surgical consideration for liver transplants, taking into account the ramifications of HPV
Prado et al., 2022[42]	2418 Subjects obtained from a systematic literature review	1277/2418	IMV drains at the confluence of the SV and the SMV: 453 subjects (18.7%) IMV drains into the SMV: 677 subjects (28%) Accessory mesenteric vein tributary to the HPV: 147 subjects (6.08%)	Brazil	Not specified	Surgical consideration for planning an operation and understanding vascularization in cases of ischemic hepatitis
Salama et al., 2010[24]	175 Liver donor subjects subjected to CT	11/175	HPV trifurcation:6 subjects (3.4%) RPPV first tributary of the HPV: 3 subjects (1.7%) Absence of RPV: 2 sujetos (1.14%)	Turkey	Male: 113 Female: 62	Surgical consideration in liver transplants
Schroeder et al., 2006[25]	250 Subjects subjected to preoperative CT	53/250	Typical bifurcation of HPV: 197 subjects (78.8%) HPV trifurcation: 38 subjects (15.2%) RAPV arises of LPV: 10 subjects (4%) LPV arises of RAPV: 3 subjects (1.2%) RAPV arises of HPV: 2 subjects (0.8%)	Germany	Male: 138 Female: 112	Surgical consideration for liver transplants in donor patients
Stagno et al., 2019[36]	1 70-year-old female subject undergoing multiple imaging examinations	1/1	The extrahepatic course of the HPV includes tributaries extending to the right upper quadrant and the abdominal epigastrium. The tributaries penetrate the liver parenchyma	Italy	Male: 0 Female: 1	Clinical consideration when giving correct treatment taking into account the embryonic development of HPV and its consequences in the patient
Watanabe et al., 2016[26]	200 Subjects subjected to CT	28/200	Typical HPV bifurcation: 172 subjects (86%) HPV trifurcation:9 subjects (4.5%) RPPV first tributary of the HPV:19 subjects (9.5%)	Japón	Male: 129 Female: 71	Surgical consideration in RPPV variant as the first tributary of HPV when performing left hepatic trisection for perihilar cholangiocarcinoma
Willmann et al., 2007[27]	60 Subjects subjected to MRI	4/60	HPV trifurcation:4 subjects (6.6%)	Swiss	Male: 39 Female: 21	Clinical consideration to take into account anatomical variations, avoiding complications in surgical procedures
Wu et al., 2007[28]	90 Subjects with liver tumors subjected to CT	15/90	Typical bifurcation of HPV: 75 subjects (83.3%) HPV trifurcation: 12 subjects (13.3%) RPV arises prematurely: 3 subjects (3.3%)	Taiwan	Male: 66 Female: 24	Clinical consideration for treatment criteria in patients with liver cancer
Zhuang et al., 2008[29]	102 Subjects subjected CT angiography	21/102	Typical bifurcation of HPV: 81 subjects (79.4%) HPV trifurcation: 15 subjects (14.7%) RAPV arises of LPV: 4 subjects (3.9%) RPPV first tributary of the HPV: 2 subjects (1.96%)	China	Male: 68 Female: 34	Surgical consideration in liver transplants, analyzing the anatomy of the donor

Table 1. Characteristics of the included studies. HPV: Hepatic portal vein, LPV: Left portal vein, RPV: Right portal vein, RPPV: Right posterior portal vein, RAPV: Right anterior portal vein, IMV: Inferior mesenteric vein, SMV: Superior mesenteric vein, SV: Splenic vein, IVC: Inferior vena cava, PPPV: Prepancreatic postduodenal portal vein, LPPV: Left posterior portal vein, CHA: Common Hepatic artery , CBD: Common bile duct , PHA: Proper hepatic artery.

formed by the confluence of three veins[9]. In some instances, the IMV drains directly into the SMV, and there are cases that feature an accessory mesenteric vein contributing to the main HPV.

Variations in the anatomical placement of the HPV are also noted. Its prevailing position is typically found posterior to the neck of the pancreas and slightly to the left of the descending portion of the duodenum, ascending within the hepato-duodenal ligament, situated posterior to the CHA and the CBD. This anatomical arrangement forms the portal triad, leading toward the hepatic hilum. Variations in the location of the HPV include the main HPV oriented anterior to the portal triad and instances of the PPPV, where the HPV is located

Type II (Trifurcation)	Type III (RPPV first tributary of the HPV)	Type IV (RAPV arises of LPV)	Isolated variations
Aboueisha et al., 2013 **16/158 (10.1%)**	Arviza et al., 2021 **31/244 (14.6%)**	Anwar et al., 2020 **16/500 (3.2%)**	Arviza et al., 2021 **4/244 (1.88%)**
Anwar et al., 2020 **8/500 (1,6%)**	Asad Ullah et al., 2020 **22/500 (4.4%)**	Arviza et al., 2021 **2/244 (0.82%)**	Asad Ullah et al., 2020 **22/500 (4.4%)**
Arviza et al., 2021 35/244 (14,3%)	Carr et al., 2003 **2/25 (8%)**	Kim et al., 2012 **1/104 (0.96%)**	Chaib et al., 2005 **1/60 (1.66%)**
Asad Ullah et al., 2020 **18/500 (3.6%)**	Covey et al., 2004 **26/200 (13%)**	Lee et al., 2008 **3/310 (0.97%)**	Salama et al., 2010 **2/175 (1.14%)**
Bogetti et al., 2001 **2/17 (11.7%)**	Gou et al., 2022 **5609/46,179 (12.15%)**	Liu et al., 2020 **92/810 (11.35%)**	Schroeder et al., 2006 **5/250 (2%)**
Carr et al., 2003 **4/25 (16%)**	Kim et al., 2012 **4/104 (3.85%)**	Schroeder et al., 2006 **10/250 (4%)**	Wu et al., 2007 **3/90 (3.3%)**
Chaib et al., 2005 **9/60 (15%)**	Koc et al., 2007 **103/1120 (9.2%)**	Zhuang et al., 2008 **4/102 (3.92%)**	Not report
Covey et al., 2004 **18/200 (9%)**	Lee et al., 2008 **20/310 (6.45%)**	Not reported	Not reported
Gou et al., 2022 **2657/46,179 (5,75%)**	Salama, et al. 2010 **3/175 (1.71%)**	Not reported	Not reported
Kim et al., 2012 **13/104 (12.5%**	Watanabe., et al. 2016 **19/200 (9.5%)**	Not reported	Not reported
Koc et al., 2007 **139/1120 (12,4%)**	Zhuang et al., 2008 **2/102 (1.96%)**	Not reported	Not reported
Lee et al., 2008 **22/310 (7.1%)**	Not reported	Not reported	Not reported
Lee et al., 2004 **4/108 (3.7%)**	Not reported	Not reported	Not reported
Macdonald et al., 2005 **6/32 (18.7%)**	Not reported	Not reported	Not reported
Salama et al., 2010 **6/175 (3.4%)**	Not reported	Not reported	Not reported
Schroeder et al., 2006 **38/250 (15,2%)**	Not reported	Not reported	Not reported
Watanabe et al., 2016 **9/200 (4.5%)**	Not reported	Not reported	Not reported
Willmann et al., 2007 **4/60 (6.6%)**	Not reported	Not reported	Not reported
Wu et al., 2007 **12/90 (13,3%)**	Not reported	Not reported	Not reported
Zhuang et al., 2008 **15/102 (14,7%)**	Not reported	Not reported	Not reported

Table 2. Prevalence articles included.

anteriorly to the pancreas and posteriorly to the duodenum. This particular variation is typically associated with abnormal dilations and coiling of the main HPV[10]. Another variant is the preduodenal HPV (Figs. 3, 4, 5 and 6).

Prevalence of HPV variants: a forest plot analysis review

In an attempt to determine the prevalence of various HPV variants reported in the literature, this review conducted four proportion forest plots, yielding the following findings:

Trifurcation Variant of the HPV: A forest plot encompassing 20 studies was conducted for this variant[7,11–29]. The analysis indicated a prevalence of 8% for HPV trifurcation, with a confidence interval ranging from 7 to 10% and a heterogeneity index of 92% (Fig. 7). For this first sample, the funnel plot graph showed significant asymmetry with a P value of 0.146, directly related to this asymmetry (Fig. 8).

Variant of the RPPV: This variant, originating from the primary, was analyzed in a forest plot incorporating 11 studies[7,13,14,16,18–21,24,26,29]. The results showed a prevalence of 7%, with a confidence interval of 4–11% and

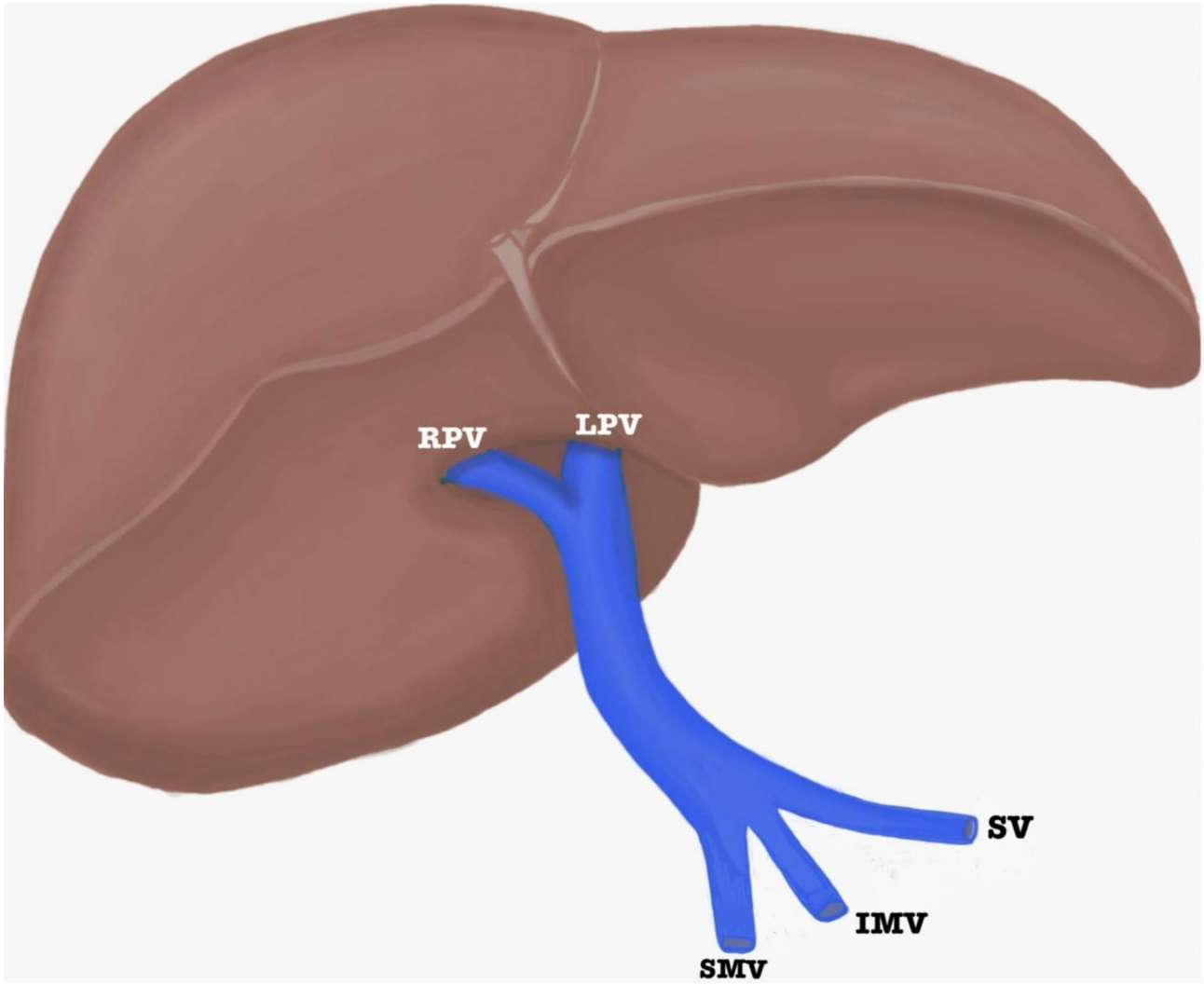

Fig. 3. Variation in the HPV origin: IMV drains at the confluence of the SV and the SMV. HPV: Hepatic Portal Vein. IMV: Inferior Mesenteric Vein. SV: Splenic Vein. SMV: Superior Mesenteric Vein. RPV: Right Portal Vein. LPV: Left Portal Vein.

a heterogeneity of 96% (Fig. 9). For this sample, the funnel plot graph showed significant asymmetry with a P value of 0.218, directly related to this asymmetry (Fig. 10).

RAPV variant arising from the LPV: Seven studies were included in the forest plot analysis for this variant[7,12,13,20,25,29,30]. The findings revealed a prevalence of 4%, with a confidence interval of 1–6% and a heterogeneity of 95% (Fig. 11). For this first sample, the funnel plot graph has showed significant asymmetry with a P value of 0.239, directly related to this asymmetry (Fig. 12).

Prevalence of Isolated Variants: The forest plot for isolated variants included data from six studies[13,14,17,24,25,28], indicating a prevalence of 2%. The associated confidence interval was 1–3%, with a heterogeneity of 97% (Fig. 13). For this sample, the funnel plot graph showed significant asymmetry with a P value of 0.136, directly related to this asymmetry (Fig. 14).

A risk of bias assessment in HPV research

In this review, 21 articles were assessed using the AQUA Checklist to evaluate the risk of bias across five domains.

Characteristics of Studies and Objective Description: All studies demonstrated strong alignment with the objectives and study characteristics, indicating consistency and reliability in this aspect.

Study Design Reporting: Of the evaluated articles, 18 presented a low risk of bias in accurately reporting their study design. However, three studies[13,19,28] exhibited shortcomings in design reporting that raised concerns about potential bias.

Methodological Characteristics: Nineteen studies showcased methodological clarity, enhancing their credibility. Conversely, two studies[20,29] exhibited methodological ambiguities, increasing the likelihood of skewed results.

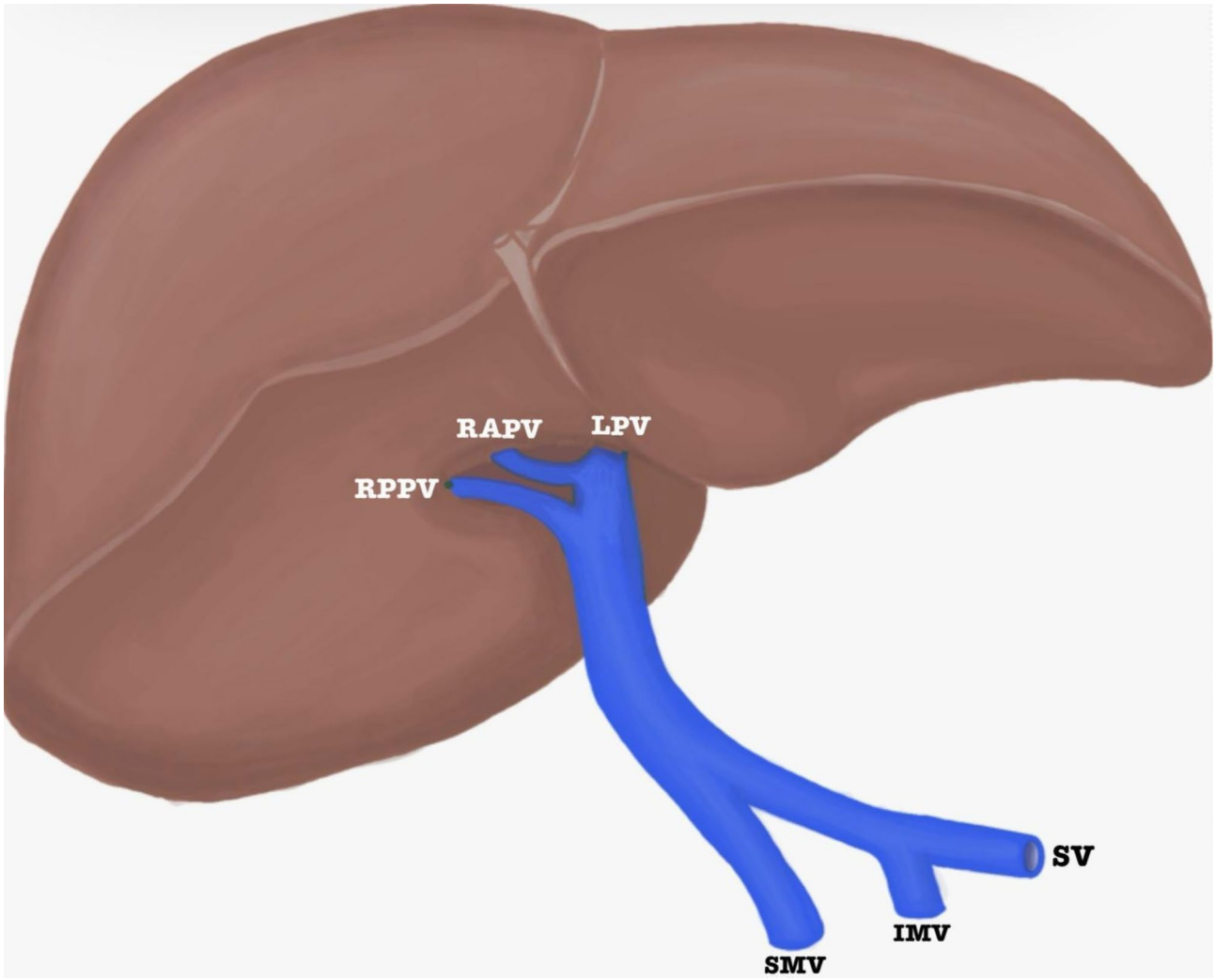

Fig. 4. Variation in the tributary patterns of the HPV: RAPV arises of LPV. HPV: Hepatic Portal Vein. SV: Splenic Vein. IMV: Inferior Mesenteric Vein. SMV: Superior Mesenteric Vein. RPPV: Right Posterior Portal Vein. RAPV: Right Anterior Portal Vein. LPV: Left Portal Vein.

Anatomical Description Accuracy: Twenty studies provided precise anatomical descriptions, ensuring accuracy in this domain. However, one study[16] relied more on eponyms than detailed descriptions, raising concerns about the preciseness of anatomical information.

Results Reporting: Fifteen studies clearly articulated their findings, enhancing the clarity and reliability of the reported results. Two studies were noted to have unclear results presentation, and five studies[12,15,21,26,27] exhibited a diffuse presentation of results in tables or within the discussion section, which might affect interpretability (Fig. 15).

In the evaluation of case report studies related to HPV research, the Joanna Briggs Institute (JBI) tool for assessing the risk of bias was employed. Eight studies that conformed to the case report methodology were included in this analysis[10,17,31–36]. Within the eight domains of the JBI tool, the majority of the studies demonstrated a low risk of bias from domains 1 to 6.

However, in domain 7, which assesses the identification and description of adverse or unanticipated events, three studies[32,34,35] did not adhere to the required reporting criteria in this domain, which could have influenced the impartiality of their findings.

Moreover, in the eighth domain, centered on the importance of providing educational value in case reports, four studies[10,32,34,36] were identified as not meeting the essential criteria for offering insightful lessons from their cases. This aspect raised questions about the study's ability to contribute constructively to the wider body of knowledge. Tables 3 and 4 contain a detailed breakdown of these findings (Tables 3 and 4).

Clinical implications of HPV variants

The anatomical variants of the HPV have significant relevance in clinical practice, especially in liver and transplant surgery. When it comes to transplant surgery, detailed knowledge of the structural and vascular anatomy of the area being treated is essential for ensuring the safety and success of liver surgery, whether it

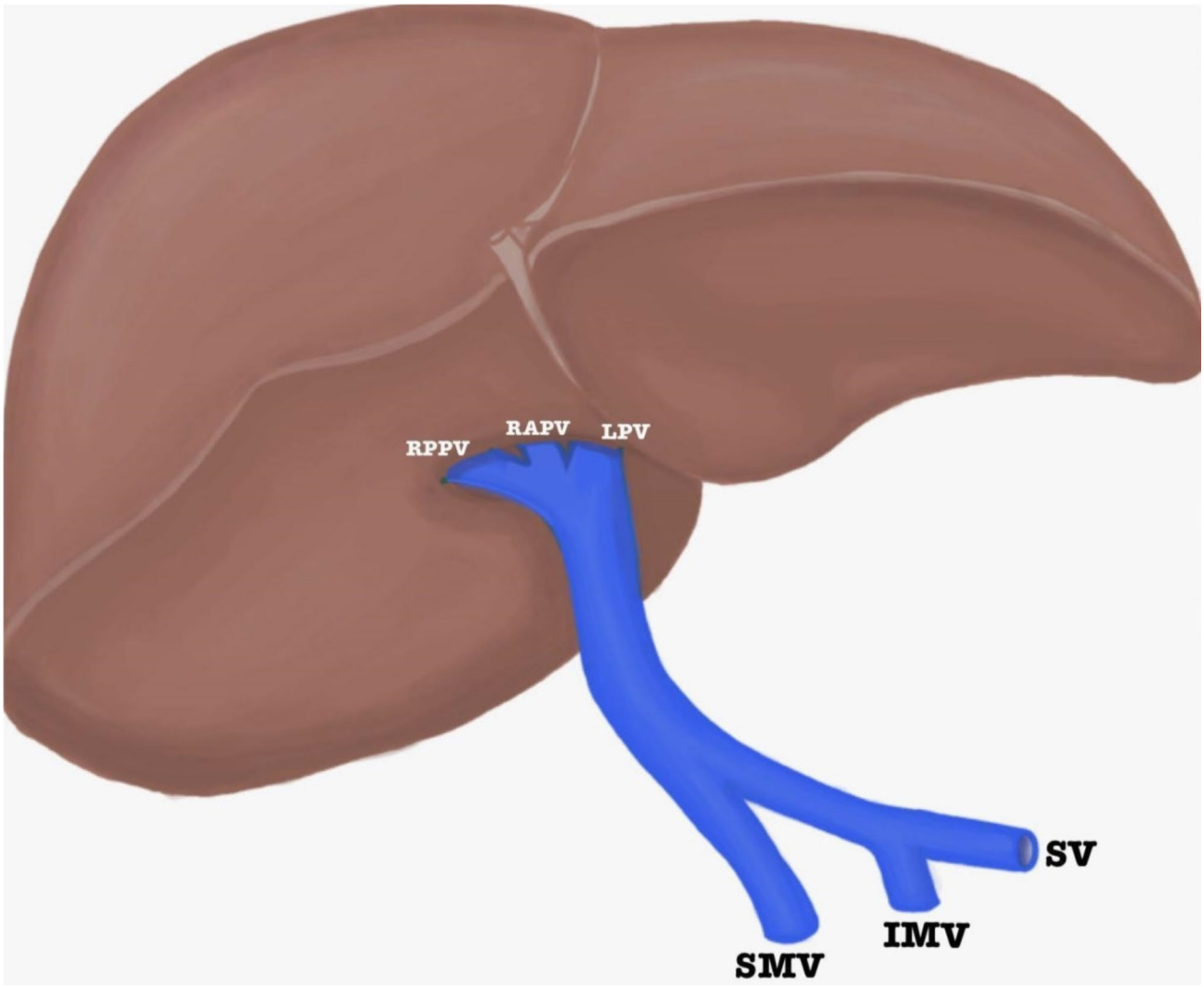

Fig. 5. Variation in the tributary patterns of the HPV: HPV trifurcation. HPV: Hepatic Portal Vein. SV: Splenic Vein. IMV: Inferior Mesenteric Vein. SMV: Superior Mesenteric Vein. RPPV: Right Posterior Portal Vein. RAPV: Right Anterior Portal Vein. LPV: Left Portal Vein.

involves removing the right or left lobe of the liver in adult recipients, or lateral sectors (segments 2 and 3), in small pediatric recipients. Therefore, this surgery must be carried out with maximum safety for both the recipient and the donor, who are healthy individuals that need to maintain proper liver function. Consequently, accurate imaging evaluations using computed tomography (CT) and magnetic resonance imaging (MRI) play a crucial role in determining the compatibility of the living donor, defining the conditions under which graft donation is not recommended, and identifying anatomical variations that could impact the surgical approach[37].

Among the various variants that may occur in the HPV system, a contraindication reported by studies for liver transplants with living donors of the right lobe occurs when the HPV lacks tributaries and directly connects with the hepatic vein in a sinuous manner, an isolated variant reported in the HPV literature. Detecting this variant through imaging in either the living donor or the recipient renders the transplant surgery unfeasible, leading to incompatibility[38].

The clinical repercussions of the HPV variations are substantial. Special attention should be paid to the early bifurcation of the RAPV and RPPV tributaries of the HPV, particularly the posterior one that may stem from the trunk, trifurcation, or LPV tributary. If, for instance, the RPPV originates at the level of the trunk, the transplant becomes complex, requiring multiple junctions (anastomoses) in the recipient's HPV and necessitating reconstruction with venous graft. This complicates the process and enhances the risk of HPV thrombosis and subsequent graft failure. Another variant that typically precludes surgery is when any of the right portal tributaries arise from the LPV, posing significant issues by affecting the portal flow of the remaining left hepatic lobe in the donor and complicating implantation in the recipient, causing incompatibility and contraindication for liver transplantation. Similarly, if the RAPV and RPPV tributaries of the HPV are situated on the left side, transplantation may also prove incompatible between the living donor and the recipient[37].

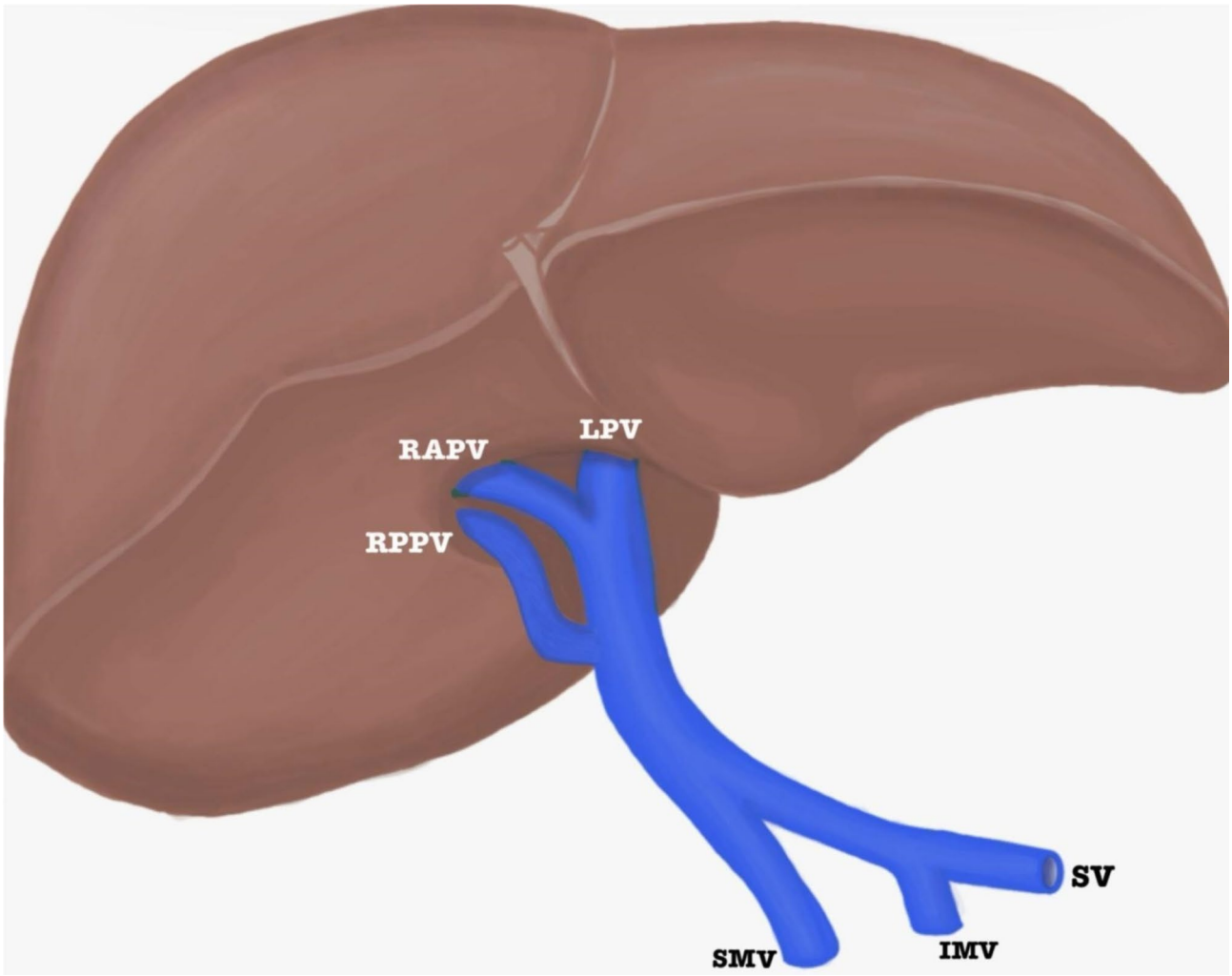

Fig. 6. Variation in the tributary patterns of the HPV: RPPV first tributary of the HPV. HPV: Hepatic Portal Vein. SV: Splenic Vein. SMV: Superior Mesenteric Vein. IMV: Inferior Mesenteric Vein. RPPV: Right Posterior Portal Vein. RAPV: Right Anterior Portal Vein. LPV: Left Portal Vein.

Another variant to consider is trifurcation, not detected correctly. In this case, if the middle tributary of the HPV is sectioned, which corresponds to one of the two right tributaries, the vascularization of the anterior or posterior segments of the donated right lobe is put at risk, which could cause a possible loss of tissue or alterations in the vascularization of the region where the variant is located[38].

However, if the HPV variants are after lobular segmentation and are correctly arranged towards each lobe, the contraindications will be minor or could even better favor the transplantation of the living donor. Finally, in the case of a transplant from a cadaveric donor, the risk factors and incompatibilities mentioned above are reduced, which makes the transplant safer and more feasible in the face of different eventualities[37].

When it comes to other procedures, such as HPV embolization, it is crucial to have a detailed understanding of the HPV angioarchitecture and detect the presence of variants. In the case of performing this procedure in the type III variant of the HPV, if the right posterior tributary originating from the main HPV is not embolized, there is a risk of causing bleeding that could result in intra-surgical complications[39].

In procedures such as trans-jugular intrahepatic portosystemic shunt (TIPS), in which a connection is established between the tributaries of the HPV and the hepatic veins, in a common HPV anatomy the procedure carries fewer risks since the locations between the two veins are close. However, in the face of variants such as type II and type III of the HPV, where there is an alteration in the intralobular and segmental location of the tributaries of the HPV, the location of the hepatic veins is not always close, which can generate complications in this procedure as it does not follow the normal disposition[39].

In addition, several studies have reported that the presence of HPV tumors, commonly referred to as leiomyosarcomas, can exert an impact on portal triad structures. However, our comprehensive review did not identify any studies that have established a definitive link between these variants and leiomyosarcoma[40]. However, in cases of liver tumors in which more than 3 liver segments need to be removed (major liver surgery), where it is necessary to occlude the HPV supply of the right or left lobe to achieve contralateral growth so that the remaining liver is of sufficient size, avoiding postoperative liver failure, in these cases it is required that the

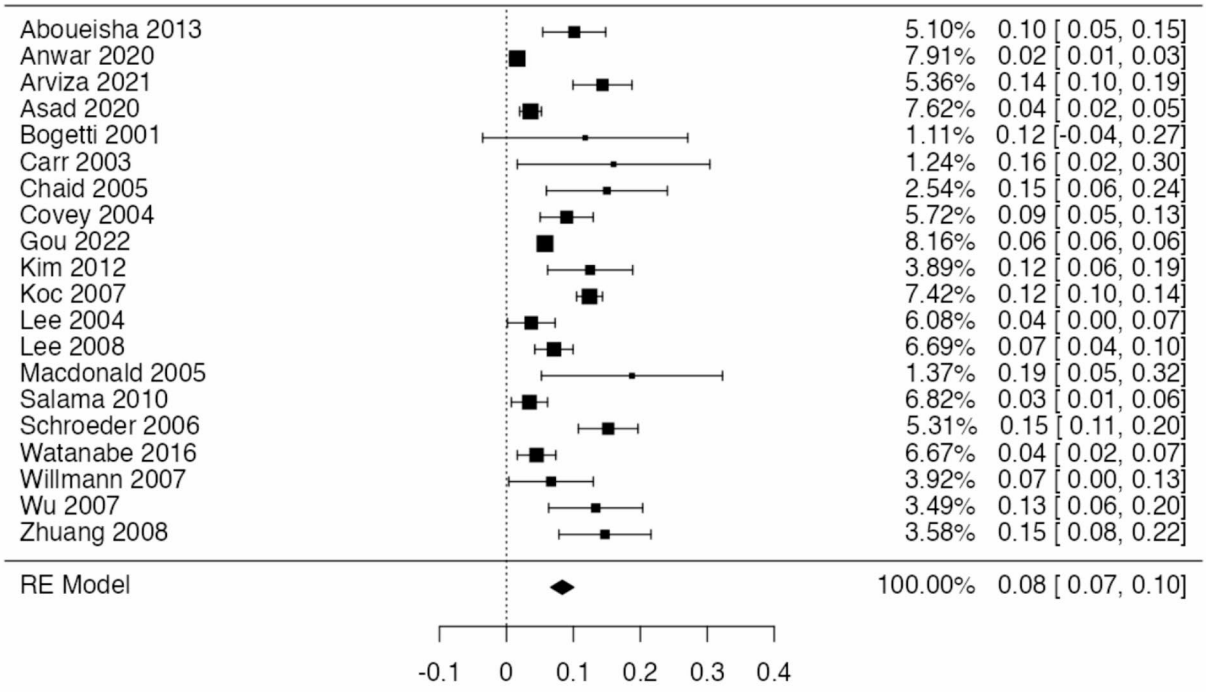

Fig. 7. Forest plot HPV trifurcation.

remaining liver be equal to or greater than 30% of the total liver volume. For this reason, all tributaries of the affected hepatic lobe must be properly occluded to allow considerable growth of the contralateral liver and obtain the best results, therefore an exhaustive study is necessary to identify the HPV bifurcations and their variants in advance, to avoid that there are tributaries without being occluded that will decrease the growth of the contralateral liver, compromising the success of the transplant[37].

In addition, patients with portal hypoplasia and sclerotic portal vein complicate transplantation because they are at high risk of thrombosis, the need for re-transplantation, or other types of invasive interventions, and experience difficulties in portal vein reconstruction during liver transplantation. Because of this, intraoperative vein thrombosis can be considered a disaster, so it is crucial to prevent this event by accurately assessing HPV morphology and blood flow through imaging, both before and during liver transplantation. For this reason, it is suggested that a HPV pressure $\geq$ 25 mmHg before graft implantation may be an objective parameter to ensure sufficient flow through the HPV, the insufficiency of which could lead to complications[41].

Discussion

This systematic review and meta-analysis aimed to elucidate the anatomo-clinical characteristics and prevalence of HPV variants, as well as their association with pathologies of the liver and adjacent structures. A key finding of our review was the correlation between the prevalence of HPV variants and various emergencies in the supra-mesocolic region, along with cases of hepatic injury.

Comparison of previous reviews on HPV variants

In our comprehensive search using specified connectors, only two reviews analyzing the variants of the HPV were identified. The review authored by Prado and Petroianu[42]reveals that HPV variants are predominantly associated with their origin, being observed in only 7% of cases. It is noteworthy that our study diverges from the exploration of variations in HPV formation, as the existing body of literature extensively covers the intricacies of HPV formation diversity. Instead, our research is specifically focused on elucidating the variants entering the hepatic hilum and conducting an in-depth investigation of uncommon variants, leading to a meticulous meta-analysis of these specific elements. In contrast, the review conducted by Stefura (2018)[43]primarily emphasizes collateral variants related to the HPV. This review, however, does not delve into the discussion of variants in HPV formation or their entry into the hepatic hilum, and it refrains from conducting a meta-analysis on these specific variants. Hence, our review takes a unique approach compared to previous studies on HPV variants. Furthermore, while we assessed eight additional reviews[2–4,44–48], their methodologies were not standardized, rendering them ineligible for direct comparison with our findings. Consequently, the comparisons were limited to the two aforementioned studies.

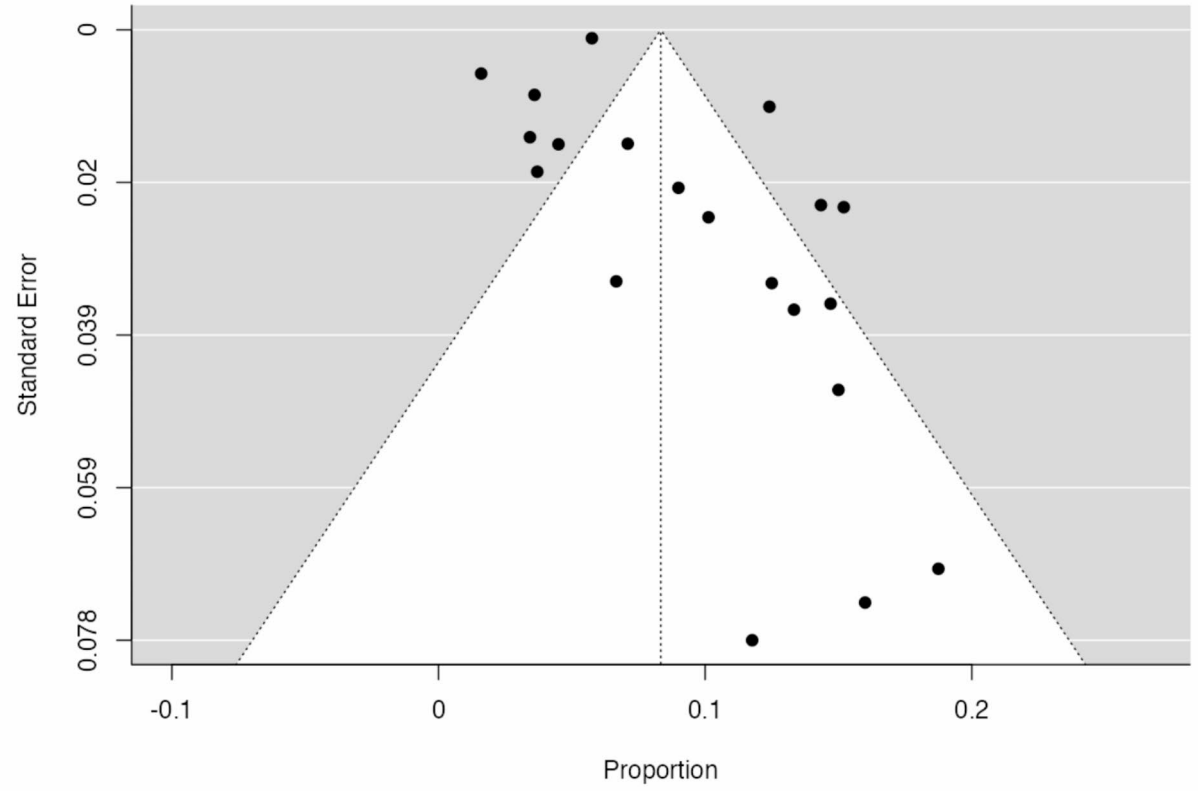

Fig. 8. Funnel plot for meta-analysis HPV trifurcation.

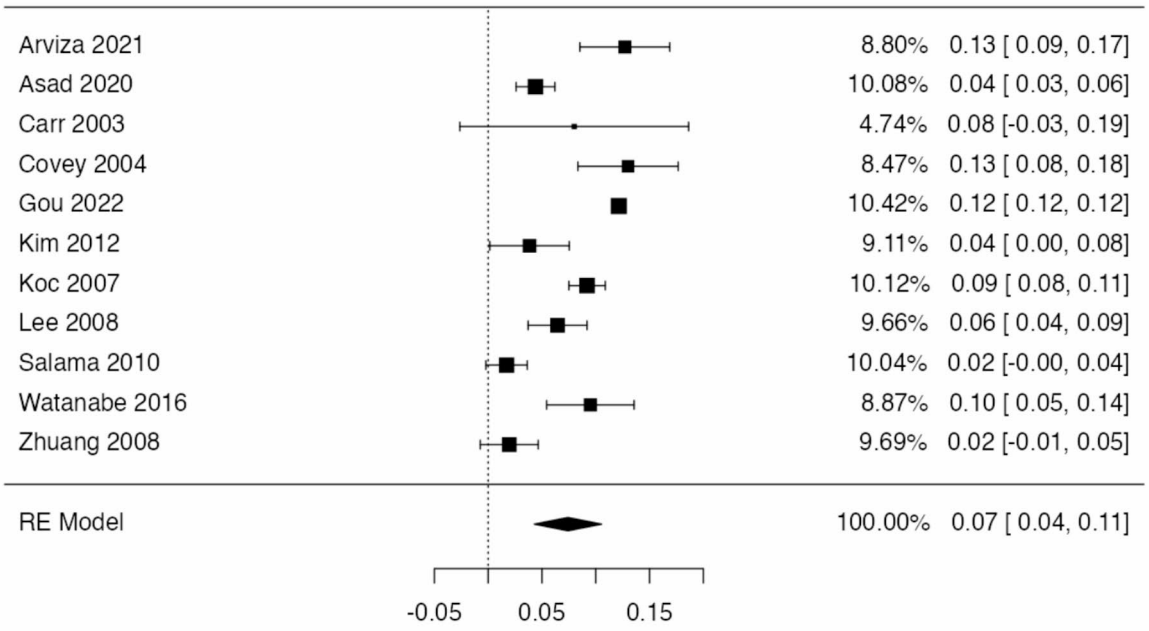

Fig. 9. Forest plot RPPV vein 1st tributary of the main PV.

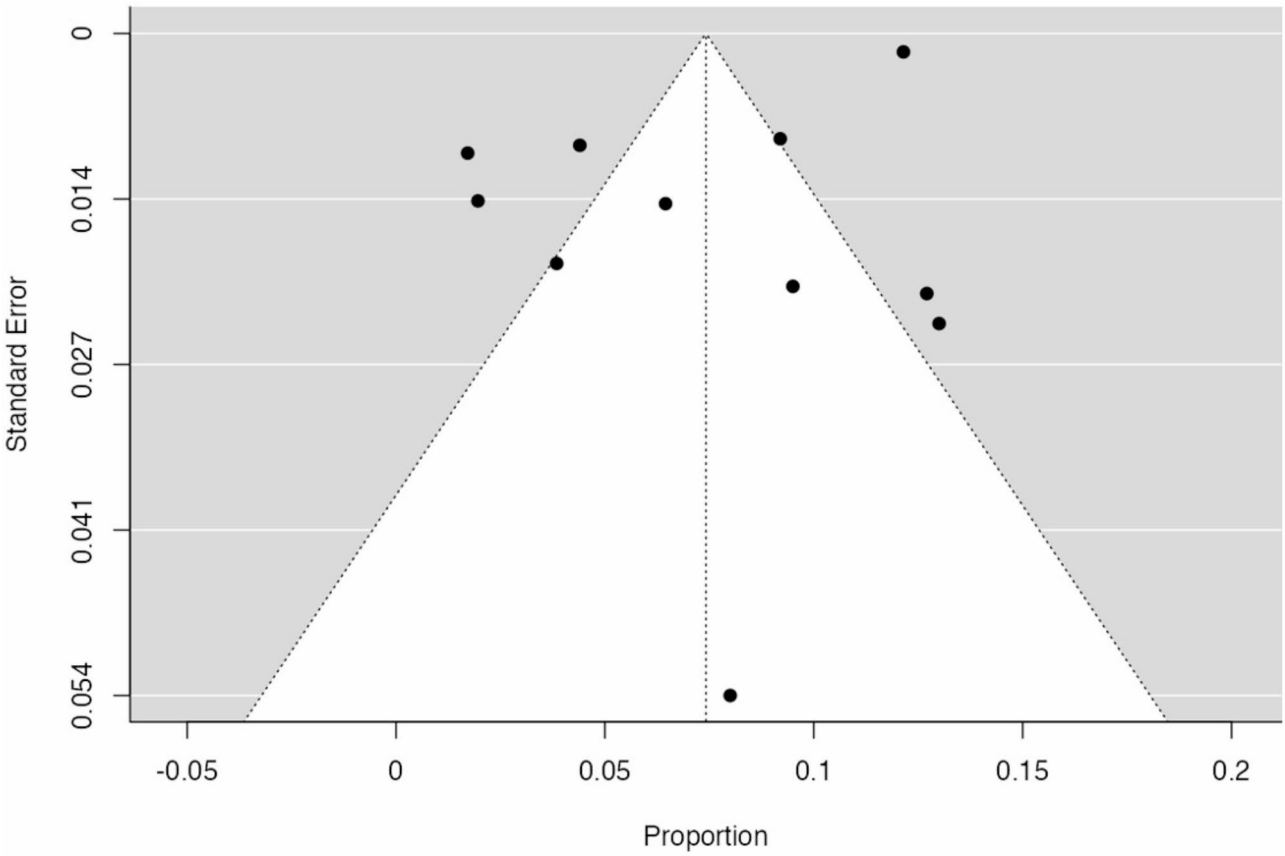

Fig. 10. Funnel plot for meta-analysis RPPV 1st tributary of the main PV.

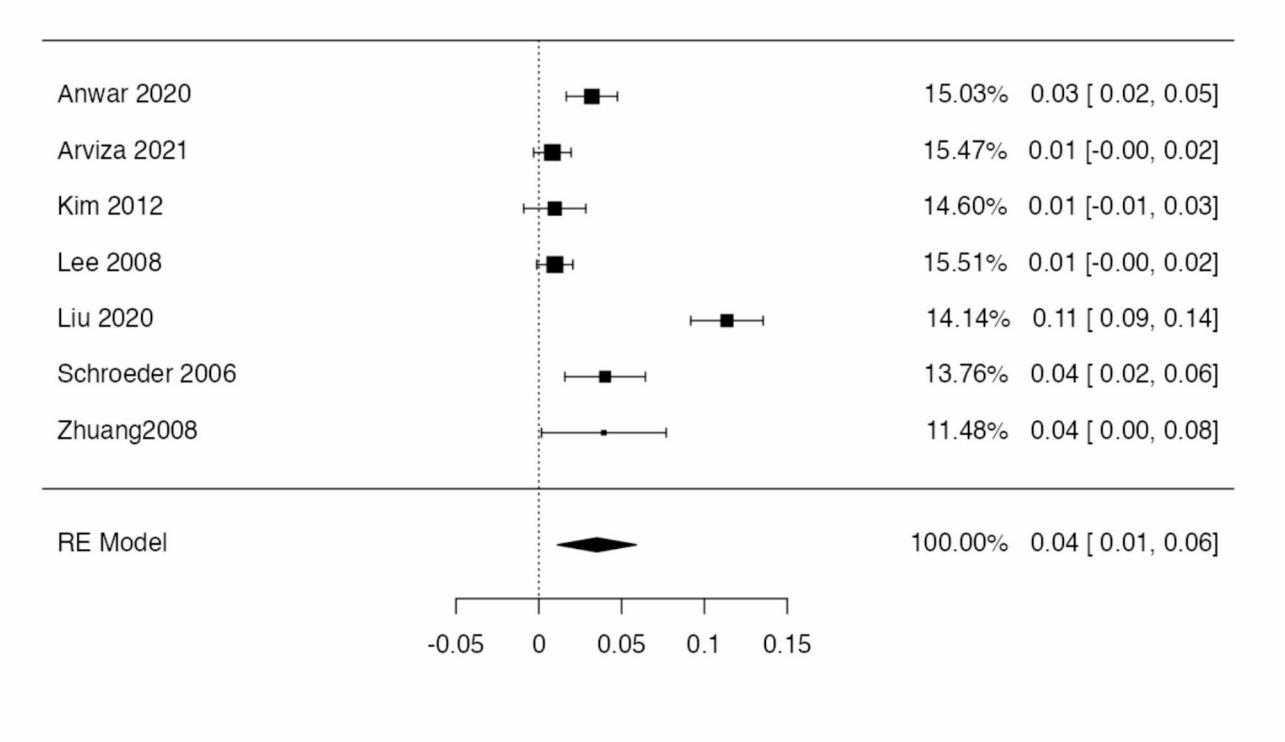

Fig. 11. Forest plot RAPV originating from the left PV.

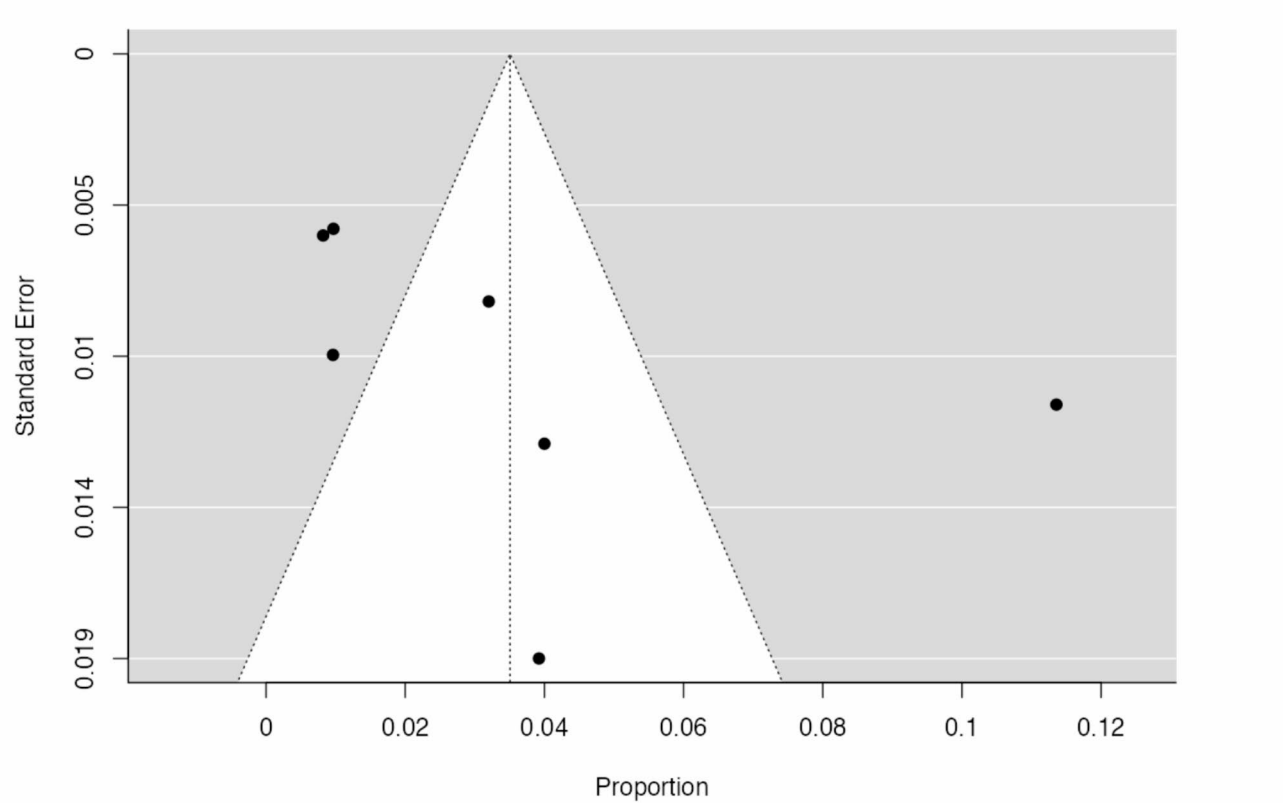

Fig. 12. Funnel plot for meta-analysis RAPV originating from the left PV.

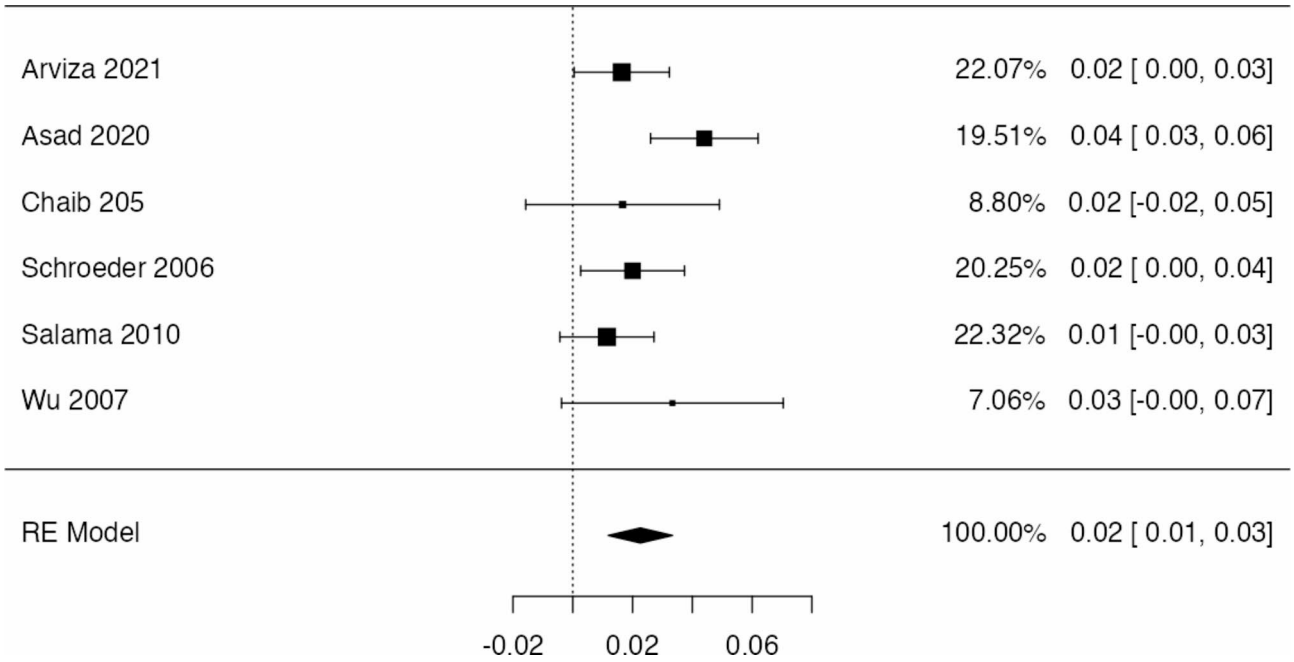

Fig. 13. Forest plot Isolated variants.

Geographical distribution and demographic factors in HPV variant studies

In the analysis of the geographical distribution of the studies included in this review, no discernible evidence suggests a correlation between HPV variants and specific ethnic or racial groups. As depicted in Fig. 2, all countries where the research was conducted are indicated. Notably, countries such as Italy, the United States,

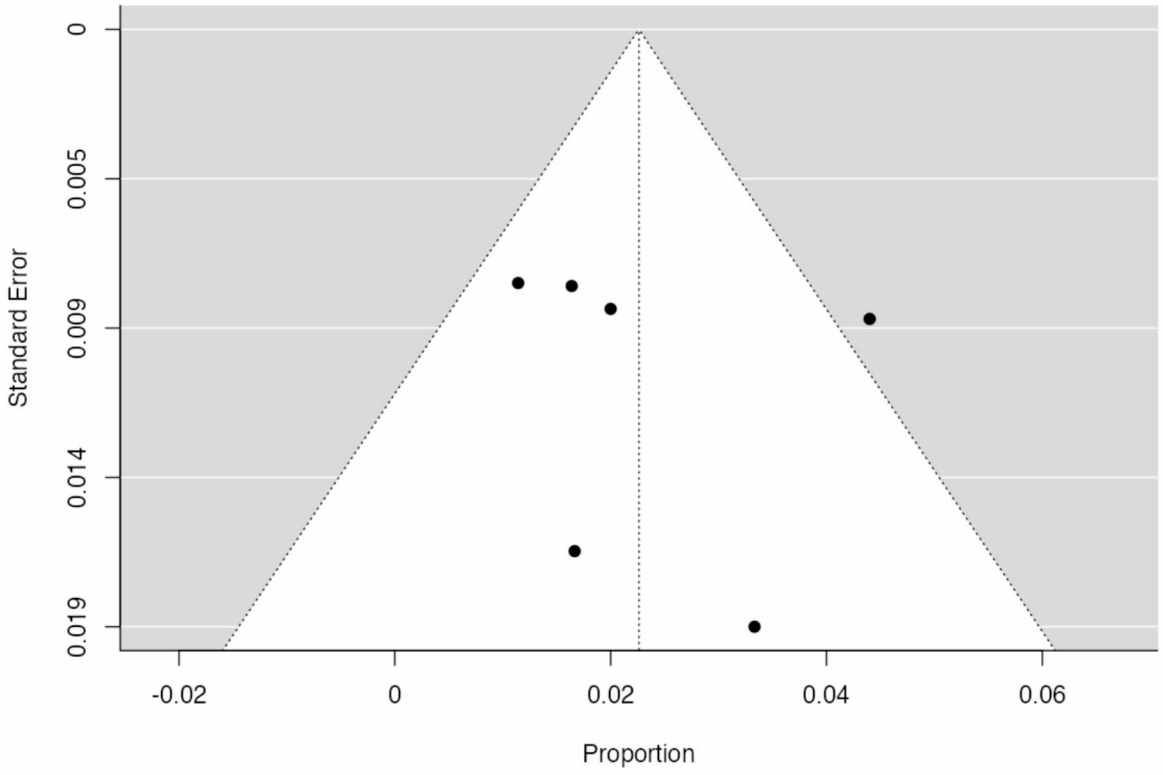

Fig. 14. Funnel plot for meta-analysis Forest plot Isolated variants.

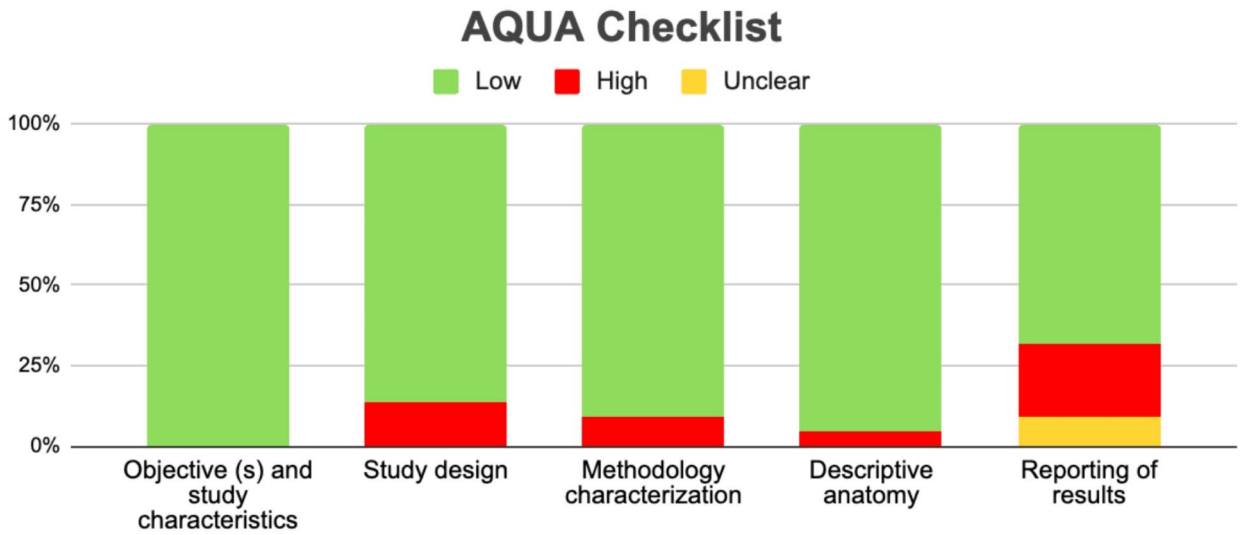

Fig. 15. Aqua checklist.

France, and India are prominently featured. Despite some of these nations being the source of bibliographic compilation works, they are also represented due to additional research originating from these locations. The age factor was not incorporated into our study's considerations. This decision was based on the congenital nature of HPV variants, which do not exhibit any correlation with the age of the participants or the onset of symptoms at a

Author	JBI Q1	JBI Q2	JBI Q3	JBI Q4	JBI Q5	JBI Q6	JBI Q7	JBI Q8	Bias risk
Akashi et al., 2023									Low
Bartsch et al., 2016									Low
Chirica et al., 2005									Low
Coulier et al., 2021									Low
Gomez et al., 2019									Low
Higashihar et al., 2022									Low
Hyidar et al., 2023									Low
Stagno, 2019									Low

Table 3. Risk of bias of included studies.

(1) Were the patient's demographic characteristics clearly described?	Yes	No	Unclear	Not applicable
(2) Was the patient's history clearly described and presented as a timeline?	Yes	No	Unclear	Not applicable
(3) Was the current clinical condition of the patient on presentation clearly described?	Yes	No	Unclear	Not applicable
(4) Were diagnostic tests or assessment methods results clearly described?	Yes	No	Unclear	Not applicable
(5) Was the intervention(s) or treatment procedure(s) clearly described?	Yes	No	Unclear	Not applicable
(6) Was the postintervention clinical condition clearly described?	Yes	No	Unclear	Not applicable
(7) Were adverse events (harms) or unanticipated events identified and described?	Yes	No	Unclear	Not applicable
(8) Does the case report provide takeaway lessons?	Yes	No	Unclear	Not applicable

Table 4. Te Joanna Briggs Institute (JBI) critical appraisal checklist for case reports.

specific age. Concerning the sex of individuals in the sample, the findings indicate no direct association of HPV variants with a higher frequency in any particular sex.

Classification of HPV variants

Additionally, the classification of HPV variants in our study adheres to the primary patterns delineated in the included studies. These patterns are initially categorized based on their entry disposition into distinct liver segments, utilizing the classification framework proposed by Lee (2008)[7]. This classification delineates the diverse patterns of blood distribution to various hepatic lobes, characterized by differing tributary formations at the lobular level. Another significant pattern identified is the trifurcation of the HPV at the entrance to the hepatic hilum, which also involves distinct lobar distribution to the liver. According to the literature, this pattern exhibits the highest prevalence in the population. Furthermore, numerous scholarly articles and textbooks extensively document the formation of the HPV as a commonly observed variant. In this article, rare variants of the HPV, which deviate from the typical path involving the duodenum and pancreas, have been detailed. Such comprehensive descriptions are pivotal for enhancing understanding and improving analyses in diagnostic and surgical contexts.

Prevalence of HPV variants

Regarding the prevalence of these variants, our focus was primarily on studies indicating a low prevalence. This approach was chosen to avoid potential overestimation of results, as including all studies might have skewed the prevalence figures. It is posited that higher prevalence rates in some studies might be attributable to non-random, intentional sample selection by authors, which could potentially distort the findings of a prevalence meta-analysis. Consequently, such studies were not included. In line with this methodology, four forest plots for prevalence were generated, revealing the following: The prevalence of HPV trifurcation was found to be 8%, with a high heterogeneity of 92%. For the prevalence of right posterior HPV variants emerging from the

main HPV, the prevalence was also 8%, with a heterogeneity of 87%, which is considered high. The prevalence of left anterior HPV variants, which originate from the left HPV, was determined to be 4%, with the analysis revealing a high heterogeneity of 95%. Finally, variants classified as isolated exhibited a prevalence of 2% and notably high heterogeneity of 97%. This high level of heterogeneity could potentially lead to an overestimation or underestimation of the reported results. Furthermore, the limited number of studies included in the meta-analysis warrants a cautious interpretation of the data presented in this study. We recommend that future research endeavors involve a larger sample size to potentially achieve greater homogeneity in the findings. For publication bias we performed an Egge regression intersection test, which is reported (Table 5; Figs. 8, 10, 12 and 14).

Clinical implications of HPV variants

Concerning the clinical implications of HPV variants, studies highlight the importance of understanding these variants before performing surgical interventions in the supra-mesocolic region. Furthermore, they emphasize the potential complications associated with transplants, especially when there is a discrepancy between the donor and the recipient regarding the presence of HPV variants[37]. For example, a contraindication reported in the literature for liver transplants with living donors of the right lobe occurs when the HPV does not present tributaries and communicates directly, in a sinuous manner, with the hepatic vein. This isolated variant, which is recommended to be identified through diagnostic imaging, can make the surgical procedure unfeasible, resulting in incompatibility for the transplant[38]. Likewise, if the RPPV originates at the level of the portal trunk, the transplant becomes more complex, since more than one anastomosis would be required in the recipient's portal system. This need for reconstruction with a venous graft increases the risk of portal thrombosis and, consequently, graft loss. On the other hand, when one of the RPV originates from the LPV, serious problems arise for the donor, since the portal flow of the remaining left hepatic lobe is impaired, also complicating the transplant in the recipient, causing incompatibility and becoming an absolute contraindication for liver transplant. Likewise, if the RPPV or RAPV are oriented towards the left side, the transplant could be incompatible, due to the complex venous anastomosis caused by the misalignment between the veins of the graft and those of the recipient, which increases the risk of thrombosis[37]. In addition, it is important to also consider the trifurcation not detected adequately; in this scenario, the section of the middle tributary of the HPV puts at risk the vascularization of the anterior or posterior segments of the donated right lobe. This situation could lead to a possible loss of tissue or alterations in the vascularization of the region where the variant is located. However, if the HPV variants are posterior to the lobular segmentation and are correctly arranged towards each lobe, the contraindications will be less or could even better favor the transplantation of the living donor[38].

In addition, patients with portal hypoplasia and sclerotic portal vein complicate transplantation as high-risk carriers of thrombosis and may require retransplantation or other types of invasive interventions. These patients also face difficulties in the reconstruction of the HPV during liver transplantation[41]. Due to these considerations, intraoperative venous thrombosis can be a disastrous event; Therefore, it is crucial to prevent it by accurate assessment of HPV morphology and blood flow through imaging, both before and during liver transplantation. In this regard, it is suggested that a HPV pressure ≥ 25 mmHg before graft implantation may be an objective parameter to ensure adequate blood flow through the HPV, whose insufficiency could lead to complications[41]. Finally, it is essential to consider the possible relationship between HPV variations and bile ducts, although specific patterns in these variants are not definitively linked; understanding variations at the level of the right lobe hepatic duct becomes essential in cases involving HPV variants[23]. This knowledge is crucial for surgical planning and execution, especially when addressing structures adjacent to the HPV. It is important to recognize that many of these HPV variants are inherent and usually asymptomatic in most patients. Consequently, medical teams must weigh multiple factors to make informed clinical and surgical decisions.

Regarding clinical issues associated with cancer, the existence of leiomyosarcomas, tumors that affect the HPV and the structures of the portal triad, stands out. Our exhaustive review did not find studies that establish a direct link between these anatomical variants and leiomyosarcomas[40]. For this reason, we consider it essential to direct future research efforts towards establishing this relationship, as it could provide valuable information on the management of these conditions. It is also important to note that in cases of liver tumors where more than three segments need to be removed (major liver surgery), it may be necessary to occlude the portal irrigation of the affected lobe to allow compensatory growth of the contralateral liver. In order for the remaining liver to be large enough to avoid postoperative liver failure, it is established that it must be equal to or greater than 30% of the total liver volume. Therefore, it is crucial that all tributaries of the affected liver lobe are adequately occluded, thus allowing significant growth of the contralateral liver and optimizing the results of the procedure. To achieve this, a thorough study is required to identify portal bifurcations and their variants in advance[37].

Another significant clinical concern often associated with HPV pathologies is portal thrombosis, a condition known for its severe complications and high risk of mortality. While our research did not establish a direct link between HPV variants and thrombotic events, we emphasize the need for early detection of these variants.

Parameter	Coefficient	St. Error	t	Sig. (2-tailed)	95% Confidence interval	
					Lower	Upper
Intercept	*0.257*	*0.4325*	*0.544*	*0.585*	*−0.811*	*1.325*
SE^B	*1.463*	*1.2334*	*1.092*	*0.307*	*−1.611*	*1.553*

Table 5. Egger's regression intercept test.

Therefore, proactive and regular monitoring of individuals with HPV variants is recommended to mitigate the risk of developing thrombotic complications[49].

HPV embolization is a technique used before a major hepatectomy to induce growth of the remaining liver by embolizing the hepatic branches that will be resected. This technique is used in patients with liver metastases in an otherwise healthy liver and in those with chronic liver disease and primary tumors. It can be performed from an ipsilateral or contralateral approach, although certain anatomical variations, such as portal vein trifurcation, complicate the contralateral procedure, especially when catheterizing branches to segments V and VI, where a reverse curve catheter is recommended[48]. Additionally, selecting the appropriate embolic material is crucial and depends on the vein diameter and anatomical access: n-butyl-cyanoacrylate is ideal for smaller veins, but requires stability in catheterization to avoid migration, while ethanol, administered through an occlusion balloon, is preferable for larger veins, though it presents challenges in cases of trifurcation. In right-sided embolization in the presence of trifurcation, the RPV does not arise from a main trunk, therefore, the tributary veins of the HPV must be embolized separately, requiring multiple catheterizations and ethanol injections. These variant increases procedural complexity, as the occlusion balloon, used for controlled ethanol administration, is relatively large and difficult to maneuver in each branch, necessitating a highly precise and meticulous technique[48–50]. For this reason, there is a risk of causing bleeding that could lead to intraoperative complications, making it essential to have a detailed understanding of the vein's angioarchitecture and to detect any anatomical variants[39]. Likewise, in procedures such as the TIPS, which establishes a connection between the tributaries of the HPV and the hepatic veins, the common portal anatomy allows the procedure to entail less risks, since the locations between both veins are close. However, in the case of variants such as type II and type III, where there is an alteration in the intralobular and segmental location of the tributaries of the HPV, the proximity of the hepatic veins is not always guaranteed. This can generate complications during the procedure because the normal anatomical arrangement is not followed[39].

Regarding the classification of HPV variants, the Thomson classification is the most prevalent, accounting for over 90% of HPV variants observed in clinical practice, with the combined three junctions (the typical bifurcation of the HPV into RPV and LPV along with a trifurcation pattern) present in more than 93% of patients. Despite being less common and constituting less than 7% of the variants, the other nine reported variations are occasionally encountered during various abdominal operations[42]. Therefore, we reiterate the importance of knowing these variants, since anatomical variations can complicate surgical procedures, particularly in abdominal and oncological surgeries, which may require modifications of standard techniques or contribute to intraoperative complications, as observed in approximately 3% of surgeries that face problems or fail in the presence of HPV variants[51]. These variations can increase the risk of iatrogenic injuries, such as vascular or biliary injuries, which generates greater morbidity and potentially affects patient outcomes. Thus, accurate identification of anatomical variations through preoperative imaging is crucial in decreasing the possibility of intraoperative complications and improving postoperative outcomes[51].

Bias assessment in anatomical studies

Moreover, it is important to note that the AQUA tool was employed to evaluate the bias of studies with a sample size (n) greater than 20. The utilization of the tool facilitates bias analysis in anatomical studies, revealing greater bias predominantly in the domains of study design and reporting. Despite the critical nature of these elements in anatomical research, we consider the overall bias to be low. This assessment stems from the fact that only a limited number of the included studies demonstrated a notable risk of bias within these domains. Furthermore, in the case of studies featuring case reports with a sample size not exceeding 20, we employed the JBI tool for evaluation. The analysis indicated a higher risk of bias across most studies, attributable to a lack of consistent and clear clinical correlations in many anatomical studies. However, given their anatomical focus, we believe that this type of bias does not significantly impact the methodology of the included studies.

Limitations

The limitations of this review were the publication and authorship bias of the included studies because studies with different results that were in non-indexed literature in the selected databases may have been excluded, the possibility of not having carried out the most sensitive and specific search regarding the topic to be studied, and finally, personal sessions of the authors for the selection of articles, all of which result in a higher probability of excluding potential cases that are not being reported in the scientific community from countries other than the Asian and North American continents.

Conclusion

Understanding the complexity and relevance of anatomical variations of the HPV was the objective of this study. We aimed to achieve this by determining the prevalence of these variations and establishing their correlation with surgical and diagnostic procedures. The HPV is vital for the proper functioning of the liver. In this review, we have described that the HPV exhibits a significant number of anatomical variations. These variations are common and could be present in a substantial portion of the population. Therefore, understanding the anatomy and presence of an HPV with variations is crucial, especially in surgical procedures such as liver transplantation, hepatic tumor resection, and endovascular procedures of the hepatic hilum. The risks of not knowing the position of the intrahepatic branches of the HPV include surgical failures, intraoperative bleeding, and other iatrogenic effects in patients with this variant. With this review, we believe we have provided a detailed description of the HPV anatomy. We believe that further studies could provide a more detailed understanding of clinical presentations and more effective diagnostic and preventive management, especially for patients undergoing liver surgery. Therefore, more primary anatomo-clinical studies are needed.

Data availability

To request the data obtained in this study, you can contact the main author (Juan José Valenzuela- Fuenzalida) at the following email address; juan.kine.2015@gmail.com.

Received: 21 June 2024; Accepted: 27 November 2024
Published online: 03 December 2024

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Author contributions

Juan José Valenzuela: Protocol/project development, Data analysis, Manuscript writing/editing. Benjamin Rodriguez- Osorio: Protocol/project development, Data analysis, Manuscript writing/editing. Cristian Salgado- Torres: Protocol/project development, Data analysis, Manuscript writing/editing. Juan Sanchis- Gimeno: Data analysis, Manuscript writing/editing. Macarena Rodríguez- Luengo: Manuscript writing/editing. Pablo Nova- Baeza: Data collection or management. Mathias Orellana- Donoso: Data collection or management. Roberto Avila-Sepulveda: Protocol/project development, Data analysis, Manuscript writing/editing. Alvaro Becerra Farfan: Protocol/project development, Data analysis, Manuscript writing/editing. Alejandro Bruna- Mejias: Manuscript writing/editing. Granite Guenivere: Data analysis, Manuscript writing/editing. : Final revision and Manuscript writing/editing.Alejandra Suazo- Santibañez: Data analysis, Manuscript writing/editing. : Final revision and Manuscript writing/editing. Héctor Gutiérrez- Espinoza: Data analysis, Manuscript writing/editing. : Final revision and Manuscript writing/editing.

Funding

For this research, we have not received any funding.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-81543-3.

Correspondence and requests for materials should be addressed to H.G.-E.

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