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Comprehensive classification of anatomical variants of the main biliary ducts

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Introduction

Liver resection is the standard treatment for primary liver malignancy and selected liver metastatic disease. Advances in surgical and anaesthetic techniques have allowed surgeons to perform complex hepatic resections with low mortality rates[1] and paved the way for advances in living-donor liver transplantation (LDLT), which has seen a substantial increase in certain parts of the world. Thorough understanding and preoperative knowledge of liver anatomy, including anatomical variants of vasculature and biliary system, is paramount[2]. Complications that arise when a surgeon is unaware of their existence can be severe, with adverse impact on patient outcomes[3,4]. Historically, anatomical biliary variants (ABVs) were often underappreciated, and the prevalence is reported inconsistently in the literature. To address this, a systematic review and meta-analysis was performed to provide a comprehensive overview of the distribution of ABVs. In addition, a prevalence-based, clinically relevant classification system was constructed, which highlights the prevalence of surgically relevant ABVs.

Methods

A systematic review was performed according to PRISMA guidelines[5]. Data were retrieved from MEDLINE and Embase, using the OVID platform, until 9 September 2019. The search strategy is detailed in *Appendix S1*. Literature was considered eligible for inclusion if it was published original research and classified biliary variants according to either four or five variants, as shown in *Fig. 1*) using data from unselected patients. From included studies, country of publication, publication year, imaging method, classification method and ABV distribution were collected. Literature review and data extraction were done independently by two assessors, with discrepancy resolved by discussion. *A priori* analysis was executed, but not registered.

Data were converted to a single classification system based on ABV prevalence (*Fig. 1*) and the commonly used classification systems[6–9]. *Table S1* details how the other commonly used classifications overlap with the system proposed here. Because not all studies reported the presence of the variant in which the cystic duct (CD) joins the right sectoral duct (RSD) (5th variant), the primary analysis focused on four ABVs. For this analysis, variants other than these four were categorized as 'other'. To assess the prevalence of the fifth variant, a separate analysis was performed of studies reporting on the fifth variant. A sensitivity analysis was performed of the meta-analysis result by comparing proportions of ABVs based on imaging modalities. In addition, population analyses were done, categorizing studies into ethnic/regional subgroups based on a previously reported system[10,11] (*Table S2*). Regional subgroups were assigned based on the location of the study groups.

A multinomial logistic mixed-effects model, with study heterogeneity captured by a random intercept, was used to estimate the overall proportion of each ABV across all studies. Ninety-five per cent c.i. were used for the estimated proportion of each ABV using a parametric bootstrap with 10 000 repetitions. Here, parametric bootstrapping is a technique that uses the estimated distribution (multinomial mixed-effects logistic model) to generate additional synthetic data in order to estimate the confidence intervals[12]. Analyses were performed using custom code written in R version 3.6.0 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

The search identified 2443 studies. After removal of duplicates 1709 studies remained, and a further 1640 were excluded owing to non-relevance. Of the remaining 69 studies, 34 were considered eligible for inclusion. By assessing the references in these 34 studies, 3 more studies were included. This resulted in a final inclusion of 37 studies[6,7,9,13–46], covering a population of 12 684 for article inclusion (*Fig. S1*). *Table 1* shows the data for each included study.

The main meta-analysis, based on 12 684 patients, showed estimated proportions of type 1 ABV of 65.7 per cent, type 2 of 14.2 per cent, type 3 of 12.2 per cent, type 4 of 6.3 per cent, and 'other' of 1.6 per cent. Twenty-one studies (8204 patients) reported on

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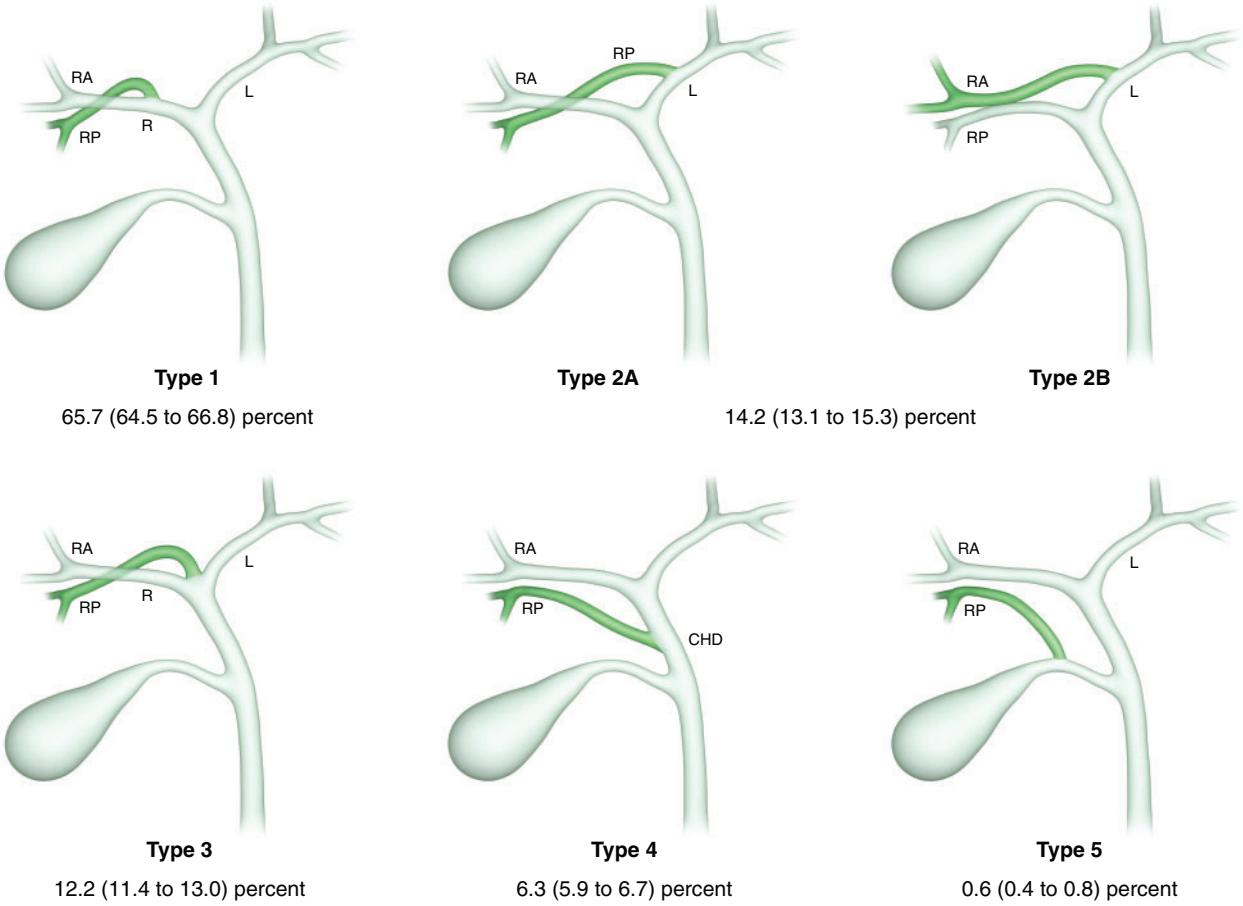

Fig. 1 Prevalence-based classification system of anatomical biliary variants

Values in parentheses are 95 per cent confidence intervals. Percentages denote the proportions estimated in the main meta-analysis. RA, right anterior; RP, right posterior; R, right hepatic duct; L, left hepatic duct; CHD, common hepatic duct.

ABV type 5, for which meta-analysis showed a proportion of 0.6 per cent (*Fig. 1*). Sensitivity analyses were performed by varying the biliary imaging modality. The direct cholangiography group (5883 patients) showed estimated ABV proportions of type 1 of 65.6 per cent, type 2 of 14.3 per cent, type 3 of 11.2 per cent, type 4 of 6.8 per cent, and other of 2.1 per cent. The MRCP group (4507 patients) showed estimated ABV proportions of type 1 of 65.4 per cent, type 2 of 13.0 per cent, type 3 of 13.8 per cent, type 4 of 6.6 per cent, and other of 1.2 per cent. *Table S3* and *Figs S2–S17* provide data and forest plots for the main meta-analyses and the sensitivity analyses.

Within the Europe, North America and Oceania region (324 patients), the estimated type 1 ABV proportion was 60.8 per cent, type 2 17.0 per cent, type 3 13.9 per cent, type 4 7.4 per cent and other was 0.9 per cent. Within the East Asia region (5683), the estimated type 1 ABV proportion was 68.8 per cent, type 2 11.0 per cent, type 3 12.8 per cent, type 4 6.3 per cent, and other 1.1 per cent. Within the South Asia region (522), the estimated type 1 ABV proportion was 56.9 per cent, type 2 21.8 per cent, type 3 9.6 per cent, type 4 5.6 per cent, and other 6.1 per cent. Within the Mediterranean basin region (273), the estimated type 1 ABV proportion was 64.8 per cent, type 2 14.3 per cent, type 3 12.8 per cent, type 4 6.6 per cent, and other 1.5 per cent. Within the Middle East and North Africa region (5882), the estimated type 1 ABV proportion was 63.5 per cent, type 2 16.1 per cent, type 3 11.2 per cent, type 4 6.2 per cent, and other 2.8 per cent.

Discussion

In this prevalence-based classification system, type 1 ABV is characterized by the right posterior sectoral duct (RPSD) joining the right anterior sectoral duct (RASD), forming the right hepatic duct (RHD). This is the standard anatomy found in 65.7 per cent of the overall population, and should not pose a problem during surgical intervention. Type 2, in which the RASD/RPSD (type 2A/2B) drains into the left hepatic duct (LHD), was found in 14.2 per cent, and is relevant during left hepatectomy, extended hepatectomy, and LDLT involving the right lobe. Type 3, the trifurcation of the RASD, RPSD and LHD, was found in 12.2 per cent, with relevance in the LDLT setting. Based on the prevalence of types 2 and 3 ABV, the authors recommend detailed delineation of biliary anatomy during left or extended hepatectomy and LDLT. Type 4, in which the RPSD that drains into the common hepatic duct, was found in 6.3 per cent; this is commonly referred to as a low insertion of the RPSD and is relevant during cholecystectomy, where it can be mistaken for the cystic duct. Type 5, characterized by the RPSD into which the cystic duct drains, was found in 0.6 per cent, and is critical in cholecystectomies where it can be injured inadvertently if mistaken for the cystic duct.

This new classification has advantages over other existing systems. First, it aims to inform uniform reporting of ABVs, creating a common ground for clinicians to convey this information clearly. Second, it focuses on clinical implications of ABVs that impact on surgical intervention, and is therefore useful clinically.

Table 1 Included literature and proportions of anatomical biliary variants

Reference	Country of publication	Region	Year of publication	Visualization method	Population	Type 1	Type 2	Type 3	Type 4	Other	
										Type 5	Other
Yoshida *et al.*[13]	Japan	EA	1996	Cholangiography	1094	739	88	194	66	5	2
Huang *et al.*[6]	Taiwan	EA	1996	Unknown	958	600	105	182	56	15	0
Cheng *et al.*[14]	Taiwan	EA	1997	Cholangiography	210	137	31	35	6	1	
Kim *et al.*[15]	South Korea	EA	2002	Cholangiography	532	403	29	58	42	0	0
Nakamura *et al.*[16]	Japan	EA	2002	Cholangiography	120	78	19	11	10	2	
Choi *et al.*[7]	South Korea	EA	2003	Cholangiography	300	197	38	32	19	6	8
Kitagawa *et al.*[17]	Japan	EA	2003	Cholangiography	180	113	26	36	5	0	
Limanond *et al.*[18]	USA	ENAO	2004	Cholangiography and MRCP*	26	19	1	5	1	0	0
Ohkubo *et al.*[9]	Japan	EA	2004	Surgical specimen	110	80	13	6	5	6	
Varotti *et al.*[19]	USA	ENAO	2004	Cholangiography	77	43	16	11	7	0	
Chen *et al.*[20]	USA	ENAO	2005	MDCT and cholangiography	56	33	10	7	5	1	
Wang *et al.*[21]	USA	ENAO	2005	CT cholangiography	62	35	11	7	9	0	
Kitami *et al.*[22]	Japan	EA	2006	CT cholangiography	158	123	19	8	5	3	
Song *et al.*[23]	South Korea	EA	2007	Cholangiography and MRCP*	111	67	8	9	22	2	3
Sirvanci *et al.*[24]	Turkey	MENA	2007	Cholangiography and MRCP*	62	43	9	6	3	0	1
Karakas *et al.*[25]	Turkey	MENA	2008	MRCP	112	61	24	16	11	0	0
Cucchetti *et al.*[26]	Italy	MB	2011	Cholangiography	200	129	24	28	16	3	
Kim *et al.*[27]	South Korea	EA	2011	Cholangiography	875	492	108	227	43	2	3
Abdelgawad and Eid[28]	Egypt	MENA	2011	MRCP	20	16	2	1	1	0	
Tawab and Ali[29]	Turkey	MENA	2012	MRCP	106	67	18	11	8	2	0
Yaprak *et al.*[30]	Egypt	MENA	2012	Cholangiography and MRCP	200	126	37	12	16	1	8
Mariolis-Sapsakos *et al.*[31]	Greece	MB	2012	Cadaveric	73	48	15	7	2	1	0
Thungsuppawattanakit and Arjhansiri[32]	Thailand	EA	2012	MRCP	163	106	15	28	9	5	
Lyu *et al.*[33]	Taiwan	EA	2012	MRCP	465	307	60	42	41	15	
Barsoum *et al.*[34]	Egypt	MENA	2013	MRCP	50	30	15	3	2	0	0
Uysal *et al.*[35]	Turkey	MENA	2014	MRCP	1011	803	42	81	73	12	
Deka *et al.*[36]	India	SA	2014	Cholangiography	299	173	52	24	20	7	23
Al-Jiffry[37]	Saudi Arabia	MENA	2015	Cholangiography	177	104	31	19	12	2	9
Takeishi *et al.*[38]	Japan	EA	2015	CT cholangiography	407	306	37	39	25	0	
Nayman *et al.*[39]	Turkey	MENA	2012	MRCP	2143	1329	245	202	149	1	217
Sarawagi *et al.*[40]	India	SA	2016	MRCP	223	124	62	26	9	2	0
Hussein *et al.*[41]	Egypt	MENA	2016	Cholangiography	248	150	44	28	16	3	7
Adatape *et al.*[42]	Turkey	MENA	2016	MRCP	1041	693	126	133	52	37	
Taghavi *et al.*[43]	Iran	MENA	2017	ERCP	362	163	48	78	13	0	60
Bauschke *et al.*[44]	Germany	ENAO	2017	Cholangiography and MRCP	103	67	17	15	2	2	0
Ulger *et al.*[45]	Turkey	MENA	2018	MRCP	200	103	49	24	16	8	
Al-Muhanna *et al.*[46]	Saudi Arabia	MENA	2019	ERCP and MRCP	150	84	43	20	2	1	0

* In the sensitivity analysis based on imaging modality, results were extracted separately based on type of imaging. EA, East Asia; ENAO, Europe, North America and Oceania; MRCP, magnetic resonance cholangiopancreatography; MDCT, multiple detector CT; MENA, Middle East and North Africa; MB, Mediterranean basin; SA, South Asia; ERCP, endoscopic retrograde cholangiopancreatography.

By simplifying ABVs based on prevalence and clinical implications, this classification system is comprehensive yet simple to use. Last, the system was devised by amalgamating the merits of previously described classification systems. To increase its utility, the regional prevalence of ABVs was also provided as an aid for surgeons in their respective localities.

Some limitations should be noted. Although the overall estimates are probably accurate representations of the prevalence, supported by the sensitivity analysis based on imaging modality, the subgroup analyses are less robust as the study size becomes considerably smaller. Further, heterogeneity within subgroups suggests that other influencing variables may exist and have not been assessed fully (such as gender or multiple ethnic origins within a study sample). As the regional subgroup classification was based on geography, it does not take into account the multiethnic nature of studied populations. Although this project covered the most common ABVs, surgeons should also be aware of the possibility of encountering other rarer, clinically relevant ABVs.

Disclosure. The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

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