Variations in morphology of cystic artery: systematic review and meta-analysis

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Abstract

Background. Variations in cystic artery anatomy are not unusual in occurrence, hence considerably crucial during hepatobiliary surgical planning and execution. This systematic review and meta-analysis of the anatomical variations of cystic artery (CA) was undertaken to emphasize their significance in surgical practice.

Methods. The PICO model was adopted, both MeSH term and free keywords were utilized for the search strategy. The risk of bias in each study was calculated by the anatomy quality assurance (AQUA) tool.

Result. The search strategy identified 8204 records, extracted 5529 studies, and evaluated 117 abstracts. Out of these 117 studies, 53 met the eligibility criteria. The CA was absent in 2% of instances (95% CI: 0.01-0.04), indicating that 98% of cases had the CA. In 10071 participants from 29 investigations, double cystic arteries were found in 13% (95% CI: 11-16%), with significant heterogeneity (I² = 91%). In 46 studies with a total of 9928 participants, 89% of the individuals had CA originating from RHA (95% CI: 85%-92%) with significant heterogeneity (I² = 94.3%) and a predictive range of 43%-99%.

Conclusion. The cystic artery is primarily derived from the right hepatic artery, followed by aberrant, proper, and left hepatic arteries. It is located anterior to common hepatic ducts and cystic ducts. The mean length and diameter of CA were 20.77 mm and 1.91 mm Short cystic arteries are common (20%) Congenital anomalies like absent CA might pose difficulty for surgeons, thus increasing the chances (prevalence 1.9%-6.62%) of on-table conversion to open cholecystectomy.

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Introduction

The cystic artery (CA) is observed to originate as the first branch from geniculate flexure of the right hepatic artery (RHA) within the hepatobiliary triangle in approximately 70% to 80% of individuals (1, 2). It then courses in a cephalic direction to ascend on the right side of the common hepatic duct (CHD), adjacent to the cystic duct, towards the gallbladder. Thereafter, it passes posterior to CHD and anterior to the cystic duct in the triangle itself, to reach and supply the gallbladder by dividing into superficial and deep branches (3). Upon reaching the gallbladder, the cystic artery bifurcates into a superficial and deep branch. The deep branch is situated within the gallbladder fossa, between the liver and the gallbladder. During laparoscopy, the CA can be observed on the video screen as it courses within the hepatobiliary triangle, positioned superiorly and slightly deeper than the cystic duct (Fig. 1). Nevertheless, it is worth noting that there are often frequent variations in this particular arrangement, with only 72% of patients exhibiting what can be considered “normal” CA anatomy.

In 1882, Carl Langebuch performed the first open cholecystectomy, later in 1985, Prof. Dr. Erich Muhe did the first laparoscopic cholecystectomy (4). Laparoscopic cholecystectomy is widely accepted for managing gallbladder stones in healthy patients. It involves a detailed dissection of CA and duct, but these structures are observed from a modified perspective on a video screen, differing from conventional methods. Arterial bleeding during laparoscopic cholecystectomy is potentially challenging due to the limited suction application and potentially impeded visual clarity due to pressure pneumo-peritoneum. Accurate visual recognition of the arterial structure surrounding the hepatobiliary triangle is crucial. The increased use of diathermy, cautery, and limited operative field of vision has led to a long learning curve of laparoscopic cholecystectomy. The anatomical variations of CA might pose difficulty for surgeons, thus increasing the chances (prevalence 1.9%-6.62%) of on-table conversion to open cholecystectomy (5, 6).

Several authors have evaluated the CA’s morphometric and morphological changes, as well as how they relate to the extrahepatic biliary system. After RHA, the common hepatic artery (CHA) most often gives CA followed by the left hepatic artery (LHA) and gastroduodenal artery (GDA). On rare occasions, the superior pancreaticoduodenal artery (SPDA), celiac trunk (CT), left gastric artery, or superior mesenteric artery (SMA) may be the source. It has been postulated that the CA may sometimes travel in advance of the CBD or CHD or, less commonly, behind them (3). Likewise, doubling of CA (2-28%) and short sturdy CA have also been reported in the literature (7, 8). The CA if arising
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from tortuous RHA (Caterpillar hump RHA) is generally short and can be avulsed in excessive traction (9). Also, abnormally long CA is seen to be associated with Caterpillar hump RHA (10, 11).

CA morphology and its connection to the extrahepatic biliary tree are revealed to be dynamic phenomena due to traction and pneumo-peritoneum. Complications after cholecystectomy, such as a biliary leak or vascular bleeding, may be caused by iatrogenic harm to the biliary tree and veins in the area. This meta-analysis was intended to provide definite information on the morphological variation of the CA and its varying connection to the duct system to reduce the complication due to wrongly ligating the CHD or CBD. With such a background, the primary objective of this study was to ascertain the prevailing source of CA. The secondary objectives were to assess the morphometric variability of CA, to ascertain the combined prevalence of variations in the number of CA and their associations, to investigate ethnic and methodological differences in CA variations.

Material and methods

The patient or problem (P); the intervention or exposure (I); the comparison intervention or exposure (C), and the clinical outcome of interest (O) (PICO) model was adopted for conducting systematic review and meta-analysis (12, 13). Both MeSH term and free keywords were utilized for the search strategy. The risk of bias in each study was calculated by the anatomy quality assurance (AQUA) tool (14).

Inclusion criteria:
1. Dissection studies
2. Intra-operative and Post-operative cholecystectomy patients
3. Radiological studies
4. Autopsy studies
5. Adult and fetal studies

Exclusion criteria
1. Case report
2. Data from the review article
3. Data from chapters or books
4. Animal studies

Search strategy and risk of bias assessment

We conducted literature search with the medical subject headings (MeSH) keywords between January 2022 and June 2023 using electronic databases including PubMed/Medline, Scopus, Web of Science, Google Scholar and CINAHL to access relevant peer-reviewed articles. The keywords were “cystic artery,” “common bile duct,” “variations,” “anomaly,” “the right hepatic artery,” “superior mesenteric artery,” “left hepatic artery,” “aberrant cystic artery,” “absent cystic artery,” “double cystic artery,” “short cystic artery,” “long cystic artery,” and “vascular variations of the gallbladder.” The keywords with Boolean operators (OR, AND, and NOT) were used to create search sequences in all possible combinations to obtain the data. The studies were shortlisted, duplicates were removed, and detailed screening of abstracts were done as per the inclusion criteria. The full text of the shortlisted studies was further evaluated based on inclusion criteria for the analysis. No time or language filters were used to narrow down the list of studies for the cystic artery or the right hepatic artery.

Data extraction and statistical analysis

The data extraction process involved the utilization of a Microsoft Excel spreadsheet. The data was extracted by two authors, encompassing essential information such as the author’s name, the population under study or country, the total sample size, the mode of investigation employed, and the outcome of interest, specifically focusing on variations of the cystic artery. The pooled weighted incidence rate of the CA originating from different sources was computed using the inverse variance method. The heterogeneity was observed by calculating I² (inverse variance) and Cochrane Q. The levels of heterogeneity, namely low, medium, and high, were assessed by quantifying the I² test statistics at 25%, 50%, and 75%, respectively. A random-effects meta-analysis model was employed to ascertain the aggregated effects in light of the considerable heterogeneity observed. The study employed forest plots to present pooled estimates along with their corresponding 95% confidence intervals (CI).

Results

The search strategy generated 8204 records. After surveying the titles and abstracts, a total of 3529 studies were extracted. Detailed screening of abstracts was done for 117 studies. Out of which only 53 studies were eligible and included in the meta-analysis, as shown in the PRISMA flow diagram (Fig. 2). These included manuscripts were published between 1917 to 2022.
Thirty Asian (7, 15-40), nine European (1, 2, 41-47), three African (48-50), two Australian (51, 52), four North American (53-56), and two South American (11, 57) studies were included. Twenty dissection studies (2,7,15,20, 27, 30, 33-37, 40, 42, 46, 47, 54, 55, 57-58), twenty-two cholecystectomy studies (1, 8, 11, 16, 18-19, 22-24, 26, 28, 29, 31, 32, 38, 41, 51-52, 56, 59, 60, 61), four autopsy (17, 43, 49, 50) and two CT studies (21, 25) were included.

The CA was absent in 2% cases (95% CI: 0.01-0.04) and double CA was present in 13% (95% CI:11-16%) with substantial heterogeneity (I² = 91%) in 10071 subjects from 29 studies. In 46 studies with a total of 9928 subjects the origin of CA was from the RHA, in 89% of subjects (95% CI: 85%-92%) with substantial heterogeneity (I² = 94.3%) and predictive interval of 43%-99%. The aberrant origin of CA is shown in Table 1. The CA was located in the cysto-hepatic triangle in 83% of cases (95% CI: 76%-89%) with significant heterogeneity (I² = 96.5%) and a predictive interval of 27%-99%.

Relation of Cystic Artery to various ducts

The position of CA in relation to CBD was overviewed in 15 studies. The CA was lying anterior to CBD in 3% of cases (95% CI: 2%-4%) followed by posterior in 2% (95% CI: 1%-4%) and inferior in 2.67% (95% CI: 2.15%-3.3%). It was mostly related anterior to CHD in 27% (95% CI: 16%-43%) followed by posterior to CHD in 21% (95% CI: 7%-48%) with high heterogeneity (I² > 90%). The relation of CA with CD is shown in Table 2.

Morphometry of Cystic Artery

The CA diameter was reported in only 2 studies (132 subjects) to be 1.91 mm (95% CI: 1.32-2.49). The length of CA was determined in six studies and was found to be 20.77 mm (95% CI: 13.95-27.58). The short trunk of CA was observed in 19.96% (95% CI: 7.86-42.17%) with substantial heterogeneity (I² = 96.2%).

Sub-group Analysis

Table 3 shows the ethnic as well as methodological distribution of origin and the number of cystic arteries. The North American studies show more aberrance in the origin of CA in comparison to other regions. Also, the cadaveric studies (Dissection) exhibit more variation in the origin of CA. Similarly, the doubling of CA has been reported more in cadaveric studies.
### Table 1. Pooled prevalence of aberrant origin of cystic artery

<table>
<thead>
<tr>
<th>Origin of Cystic artery</th>
<th>No. of subjects</th>
<th>Pooled Prevalence (%)</th>
<th>95% CI</th>
<th>No. of studies (N)</th>
<th>Higgins -I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior Mesenteric Artery (SMA)</td>
<td>2382</td>
<td>1.09%</td>
<td>0.0074-0.016</td>
<td>9</td>
<td>37.7%</td>
</tr>
<tr>
<td>Coeliac Trunk (CT)</td>
<td>1631</td>
<td>0.43%</td>
<td>0.002-0.009</td>
<td>5</td>
<td>Nil</td>
</tr>
<tr>
<td>Common Hepatic Artery (CHA)</td>
<td>3154</td>
<td>2.33%</td>
<td>0.0125-0.0427</td>
<td>14</td>
<td>86.4%</td>
</tr>
<tr>
<td>Proper Hepatic artery (PHA)</td>
<td>1987</td>
<td>5.02%</td>
<td>0.0306-0.0813</td>
<td>14</td>
<td>83%</td>
</tr>
<tr>
<td>Proper hepatic artery bifurcation (PHA bf)</td>
<td>772</td>
<td>5.55%</td>
<td>0.017-0.1641</td>
<td>3</td>
<td>77.7%</td>
</tr>
<tr>
<td>Aberrant Right hepatic artery (ab RHA)</td>
<td>5076</td>
<td>6.29%</td>
<td>0.0426-0.092</td>
<td>19</td>
<td>89.6%</td>
</tr>
<tr>
<td>Left hepatic artery (LHA)</td>
<td>3421</td>
<td>4.04%</td>
<td>0.0281-0.0577</td>
<td>16</td>
<td>61.1%</td>
</tr>
<tr>
<td>Gastroduodenal artery (GDA)</td>
<td>4969</td>
<td>3.61%</td>
<td>0.0266-0.0488</td>
<td>22</td>
<td>73.8%</td>
</tr>
<tr>
<td>Superior Pancreatico-duodenal artery (SPDA)</td>
<td>1731</td>
<td>0.29%</td>
<td>0.0012-0.0069</td>
<td>5</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Table 2. The position of cystic artery in relation to cystic duct

<table>
<thead>
<tr>
<th>Relation of cystic artery to cystic duct</th>
<th>No. of subjects</th>
<th>Pooled estimate (95%CI)</th>
<th>No. of studies</th>
<th>Higgins -I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anteriorly</td>
<td>6790</td>
<td>23% (95% CI:8%-51%)</td>
<td>22</td>
<td>98.8%</td>
</tr>
<tr>
<td>Superiorly</td>
<td>673</td>
<td>10% (95% CI: 2%-36%)</td>
<td>4</td>
<td>98.1%</td>
</tr>
<tr>
<td>Inferiorly</td>
<td>2460</td>
<td>6% (95% CI: 4%-9%)</td>
<td>8</td>
<td>73.0%</td>
</tr>
<tr>
<td>Posteriorly</td>
<td>5141</td>
<td>4% (95% CI:1%-11%)</td>
<td>12</td>
<td>98%</td>
</tr>
</tbody>
</table>

* CI: confidence interval
Table 3. Summary of sub-group analysis of cystic artery.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Ethnic or geographical distribution</th>
<th>Methodological distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asian</td>
<td>Australian</td>
</tr>
<tr>
<td></td>
<td>RHA</td>
<td>0.9002 (0.8583; 0.9391)</td>
</tr>
<tr>
<td></td>
<td>RHA</td>
<td>0.9002 (0.8583; 0.9391)</td>
</tr>
<tr>
<td></td>
<td>abRHA</td>
<td>0.0411 (0.0256; 0.0653)</td>
</tr>
<tr>
<td></td>
<td>PHA BI</td>
<td>0.0694 (0.0292; 0.1562)</td>
</tr>
<tr>
<td></td>
<td>LHA</td>
<td>0.0330 (0.0185; 0.0582)</td>
</tr>
<tr>
<td></td>
<td>PHA</td>
<td>0.0336 (0.0151; 0.0729)</td>
</tr>
<tr>
<td></td>
<td>CHA</td>
<td>0.0197 (0.0515; 0.1580)</td>
</tr>
<tr>
<td></td>
<td>Coeliac A</td>
<td>0.0053 (0.0020; 0.0141)</td>
</tr>
<tr>
<td></td>
<td>GDA</td>
<td>0.0363 (0.0225; 0.0579)</td>
</tr>
<tr>
<td></td>
<td>SPDA</td>
<td>0.0031 (0.0008; 0.0122)</td>
</tr>
<tr>
<td></td>
<td>SMA</td>
<td>0.0143 (0.0088; 0.0232)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>0.02 (0.008; 0.062)</td>
</tr>
<tr>
<td></td>
<td>Double</td>
<td>0.1190 (0.0867; 0.1611)</td>
</tr>
</tbody>
</table>

*Value in square bracket are (95% CI), RHA; Right Hepatic Artery, ab; Aberrant, A; Artery, PHA; Proper Hepatic Artery, LHA; Left Hepatic Artery, CHA; Common Hepatic Artery, GDA; Gastroduodenal Artery, SPDA; Superior Pancreatico-duodenal Artery, SMA; Superior Mesenteric Artery. ** NR- Not Reported.
Discussion

Embryology

Anatomical variations of the CA may be justified by looking at the early embryological developmental period. In the third week of intrauterine life, cells from the splanchnic mesoderm migrate below the lateral plate mesoderm and give rise to a pair of dorsal aortas. Signal proteins such as Sonic hedgehog (SHH) and vascular endothelial growth factor (VEGF), expressed by the notochord cause the fusion of two dorsal aortas to form descending aorta (62, 63). The dorsal aortae give rise to several vitelline arteries. The CA develops from the seventh and eighth ventral segments in the 4-week-old embryo and descends caudally to reach the lower thoracic region. The superior mesenteric artery arises from the ventral segments of the ninth, tenth, eleventh, twelfth, and thirteenth vertebrae, with the thirteenth segmental being the main source. The displacement occurs during the latter part of the second month of embryonic development, commonly referred to as “caudal wandering.” The early phases of the process entail a posterior movement aided by an unrestricted connection along the length of the ventral segments at different points. The observed caudal shift is ascribed to varying growth rates in the ventral aorta’s vicinity (64). These arteries regress after birth except the 10th, 13th, and 21st vitelline arteries, to develop into the major ventral branches of the aorta that supply the gut.

The existence of notable anatomical variations can be attributed to the ventral longitudinal anastomosis that connects the ventral segments, ultimately giving rise to celiac or superior mesenteric artery branches. The development of significant anatomical variations is contingent upon the temporal and spatial resorption of the longitudinal anastomosis and ventral segmental roots. Failure of regression of some vitelline vessels may lead to extensive cystic artery variation (62). Additionally, the profound growth of liver and rotation of stomach may disturb the hepatobiliary vasculature arising from coeliac trunk in the central axis of aorta affecting the relation and position of the CA (59). The authors propose that there is a possibility of minor variations arising from similar connections between branches of the arteries mentioned earlier, especially in situations where there is a widespread network of small blood vessels in the vascular system of the gastrointestinal tract.

The CA is that vital structure which is ligated during laparoscopic cholecystectomy. With the rapid onset of minimally invasive cholecystectomy techniques, such as natural orifice transluminal endoscopic surgery (NOTES) and single incision laparoscopic cholecystectomy (SILC) the variations in CA form the most crucial relation with the hepatobiliary duct system, therefore is identified as a very common cause of profuse bleeding during these procedures (61). The CA usually arises from the RHA (Fig. 1) and frequently passes posterior to the CHD within the hepatobiliary triangle, where it lies superior to the CD.

The origin of the CA is highly variable. The most common variant origin is from the hepatic artery proper when it often crosses anterior to the CBD or CHD to reach the gallbladder. Rarely, it may arise from the left hepatic, gastro-duodenal, superior pancreaticoduodenal, coeliac, right gastric, or superior mesenteric arteries; in these cases, the CA may not traverse the hepatobiliary triangle (3). This meta-analysis showed 89% (95% CI: 85%-92%) of CA originated from RHA and the rest were atypical. Also, CA were noted to be absent in 2% of cases (95% CI: 0.01-0.04). In such congenital absence of CA, the gall bladder is noted to be supplied by the liver parenchymal arterial vessels, such anatomic variants increase the risk of arterial injuries during surgery if unrecognized by the surgeon, then, leading to intra-operative hemorrhage and might also complicate as hepatic artery thrombosis (65, 66, 67).

Loukas et al. (68) reported the coexistence of a double CA originating from both the RHA and the posterior superior pancreaticoduodenal artery. Occasionally, the CA exhibits a bifurcation in close proximity to its point of origin, resulting in the formation of two distinct vessels, commonly referred to as Double CA (2, 5). Alternatively, it is possible for an accessory CA to originate from the hepatic artery (Fig. 3) or one of its branches. Ethnic disparities in the prevalence of double CA have been observed (49). The Australian population exhibited the highest prevalence of double CA, with a rate of 22% (95%CI: 14.95%-31.16%). Furthermore, the dissection studies revealed a higher incidence of double CA compared to cholecystectomy cases. There was a statistically significant difference observed between the two techniques, namely laparoscopic and open procedures, with rates of 10.24% (95% CI: 7.79%-13.34%) and 14.13% (95% CI: 12.39%-16.07%), respectively.
CA is the first structure that is encountered during laparoscopic cholecystectomy. Sometimes CA is located outside the triangle, in such cases the vessel in this triangle is the RHA (3). In this meta-analysis, CA was located outside the cysto-hepatic triangle in 17% of cases. In such cases, there are more chances that CA lies anterior to cystic duct (Fig. 4). The CA that lies anterior to CD is more prone to injury in dissection during cholecystectomy. We found that the CA was mostly related to all the hepato-biliary ducts throughout its course. Therefore, there is a risk of a biliary leak if the CA courses anterior to the CHD or CBD due to frequent handling with the forceps during cholecystectomy (41, 69).

The CA is usually less than 3 mm in diameter, and a larger artery in the hepatobiliary triangle is more likely to be the RHA (3). The mean length of the CA was 16.9 mm ranging between 2 mm and 55 mm) (7). M. Taimur et al and De Silva reported unusually long CA (mean length = 23 mm) (39, 70). In this meta-analysis, we found the mean diameter to be 1.91 mm (95% CI: 1.32-2.49) which was very less than normal and therefore can be confused with the small caliber vessels (i.e., ductal arteries). Also, we found that the length of CA was more, which might be a warning sign for Caterpillar hump (9, 11). If caterpillar hump of RHA gives rise to CA it has a very short trunk and is very prone to avulsion during surgical procedures. Sometimes, abnormally large cystic artery may mimic an aberrant hepatic artery which may accidentally be ligated (1).

Clinical implication

Intraoperative recognition of variations in CA is crucial to minimize catastrophes while operating in the hepatobiliary triangle. The presence of a tortuous variant RHA that bends within this triangle can lead to misidentification as either a sizable CA or the CD (64). Consequently, there is a risk of inadvertently clamping this artery while ligating the CD. The positioning of the CA, RHA, or common hepatic arteries in relation to the biliary tree exposes them to potential risks, especially while incising the peritoneum covering the hepatoduodenal ligament during cholecystectomy. The occurrence of hemorrhage resulting from unintentional damage to these variant vessels can pose challenges. However, the hasty attempts to control the bleeding through the inadvertent use of a clamp or forceps lead to the most significant complications, as they cause furthermore injury to the underlying biliary tree (71).

Limitations of the study

This meta-analysis has few limitations such as no data were reported based on gender and age distribution of CA variations. Also, the only the geographical locations of patients and cadavers were analysed without any consideration of the actual racial and ethnic differences.

Conclusion

This meta-analysis is amalgamation of the information in the literature on the anatomical variations of the cystic artery. According to our analyses, the cystic artery most commonly originates from right hepatic artery followed by aberrant right hepatic, proper hepatic, and left hepatic artery. There are other rare point of origin which are very less common. The cystic artery is located anterior to the common hepatic duct, common bile duct, and cystic duct. A short cystic artery 19.96% (95% CI: 7.86-42.17%) and mean diameter of the cystic artery was determined to be 1.91 mm (95% CI: 1.32-2.49). Although, the congenital anomalies like absent and double cystic artery had very low prevalence but have to be kept in mind while operating. Furthermore, the prevalence of variations was observed to be more in dissection studies, this could be due to manual handling of the specimens. Knowing about all these variations is very crucial for hepato-biliary surgeons for the reason that the cystic artery is the first structure which is dissected and ligated in laparoscopic biliary surgeons for the reason that the cystic artery is the first structure which is dissected and ligated in laparoscopic cholecystectomy. This will definitely prevent the inadvertent injury to vessels as well as ductal system therefore preventing intra-operative and post-operative complications.

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Disclosure of interest

The authors declare that they have no competing interest.

Author’s contribution

The concept of the study was given by Adil Asghar. The study design, material preparation, data collection was done by Adil Asghar and Ananya Priya. The analysis was done by Adil Asghar. The manuscript preparation and proof reading was done by all the authors.

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