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Clinical significance of morphological variations of the inferior phrenic arteries

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Abstract

The rapid development of sciences such as genetics and molecular biology offers hope that better therapeutic methods can be developed and diagnosis and treatment made more effective. However, we must not forget that the basis for understanding the complex mechanisms of diseases and associated symptoms is knowledge of the relevant location and correlation among organs. In the present study, we focus on the clinical significance of the inferior phrenic artery. The diaphragm is a muscular structure that separatesthe abdominal and chest cavities. Thanks to this position, the inferior phrenic artery is much more significant than formerly assumed. A rich network of collaterals makes this vessel important in the development of neoplasms and metastases. Knowledge of anatomical variants of the inferior phrenic artery is also crucial for radiological procedures such as embolization. The main aim of this study is to review the involvement of the inferior phrenic artery in physiological and

pathophysiological processes. This work has value for all practicing doctors, especially radiologists and surgeons.

Key words: inferior phrenic artery, diaphragm vascularization, morphological variations, accessory inferior artery, hepatocellular carcinoma, pseudoaneurysm, embolization

INTRODUCTION

The diaphragm is a dome-shaped muscular structure that separates the thoracic and abdominal cavities(5). It is vascularized from several sources. Its cranial side is supplied by the pericardiacophrenic, musculophrenic,and superior phrenic arteries(32). However, the main donors of arterial blood to the diaphragm are the inferior phrenic arteries(IPAs)(5). In the most common anatomical pattern, these vessels branch off the abdominal aorta. Each then crosses the crus of the diaphragm. The IPAs are located on the abdominal surface at an angle. Each vessel then divides into ascending and descending branches. The bifurcation is near the dorsal part of the central tendon of the diaphragm(21). The ascending branch creates anastomoses with other arteries that supply the organ, namely the musculophrenic andpericardiacophrenic arteries and the same vessels on the opposite side(21). The ascending branch of the left inferior phrenic artery(LIPA) crosses behind the esophagus. It is then located on the left side of the aortic hiatus. The ascending branch of the right inferior phrenic artery(RIPA) runs behind the inferior vena cava. Thereafter, it is located on the right side of the vena cava foramen(21). The descending branches of the IPAs anastomose with branches of the 8th to 12th intercostal arteries and the musculophrenic artery(5).

The provision of fresh arterial blood rich in oxygen is a precondition for keeping every organ alive(36). The RIPA and LIPA are the most important sources of arterial blood for the diaphragm. This is highly physiologically significant because the diaphragm is crucial for respiration. It enables the thoracic cavity to expand during inspiration so that fresh air reaches the chest. Moreover, it prevents the withdrawal of gastric contents from the stomach into the esophagus by occluding the gastroesophageal junction(5). Branches of both the RIPA and LIPA also supply other organs such as the stomach, spleen, and esophagus(37).

Anatomical variations of the RIPA and LIPA are well-known. Arteries often branch off abdominal arteries such as the gastric and renal arteries. The most common variant for both

IPAs is an origin from the celiac trunk. Interestingly, they can originate independently or via a common trunk(2, 3, 6, 7, 21).

Apart from providing blood to the diaphragm, the IPAs are also implicated in pathological conditions including pseudoaneurysm. The rupture of an IPA is life-threatening and requires early diagnosis and treatment(32). Moreover, IPAs are particularly involved in the formation of extrahepatic collateral pathways that especially supply hepatocellular carcinomas(7). They are also important in disorders caused by thoracic trauma, such as hemothorax(1).

The aim of this study is to assemble current knowledge about the physiological and clinical importance of IPAs and their anatomical variants. An important part of this review is the description of clinical syndromes related to these vessels. This knowledge is necessary for clinical practice, especially for radiologists and surgeons performing procedures pertaining to IPAs such as embolization.

Anatomical variants

Various types of IPA origin have been thoroughly described in recent studies.Aslaner et al.(2) proposed an interesting division of these arteries, distinguishing two main groups:

- arteries originating independently without a trunk (Table1)
- arteries originatingviaa common trunk(Table2 and Table3)

The tables present the frequency of each type according to previous investigations.The papers by various researchersdiffer in the number of cases analyzed, the type of arterial detection method, and the classification system (2, 3, 6, 7, 17, 21, 38)

Aslaner et al.(2) examined 1190 patients by abdominal computed tomography angiography(CTA). The images assessed included those obtained from patients with histories of mesenteric ischemia, peripheral arterial disease, renal artery stenosis, and aortic aneurysm and donors for renal transplantation. Patients with histories of hepatocellular carcinoma, liver disease, or severe atherosclerosis and those who had undergonetransarterial chemoembolization orendovascular or surgical treatment of the aorta were excluded from this investigation. Each image was assessed for IPA origin by radiologists, followed by statistical analysis(2). Their classification was very accurate. This is the only study that described four

possible origins of the RIPA and LIPA via a common trunk(Table1).Greig et al.(6) examined 425 cases by dissection. American whites and blacks of both sexes were included in their study, which described all the patterns of arterial derivation found. Interestingly, Greig et al. (6) described a LIPA branching from the accessory left hepatic artery and a RIPA originating from the accessory right hepatic artery and spermatic artery. These variants have not been described elsewhere.

Kimura et al.(17) analyzed the type of origin of RIPA only. They examined 178 patients with hepatocellular carcinoma who required transcatheter arterial chemoembolization via the RIPA. They used angiography to detect the origin pattern and relationship of the vessel to the celiac, superior mesenteric, and right renal arteries. They described a RIPA arising from the dorsal pancreatic artery. This type has not been reported in other investigations.

Gürse et al.(7) examined 26 cadavers (24 male and two female) by classical anatomical dissection. They resected the diaphragm, abdominal aorta, both kidneys, and the suprarenal glands in order to visualize the course of the IPAs. Their dissection also revealed branches of the RIPA and LIPA.

Szewczyk et al.(37) dissected the upper abdominal regions of 48 Caucasian cadavers (29 males and 19 females). All the specimens were free of trauma, pathology, or prior surgery in the upper abdominal organs. The authors examined the origins of the LIPA and RIPA and their diameters.

Loukas et al.(21) examined 300 adult human cadavers (120 female and 180 male) by dissection. They excised the inferior vena cava, liver, superior and inferior mesenteric arteries, stomach, pancreas, and celiac and superior mesenteric nerve plexuses. This allowed a clear field of visualization to be obtained. The spleen, both kidneys, and the suprarenal glands were not removed. In this study, the termination of the IPAs was also examined. The diameter of each IPA was measured. Interestingly, the authorsdescribed a case of aLIPA branching from the proper hepatic artery. Thishas not been seen in other studies(21).

Basile et al.(3) examined 200 patients with hepatocellular carcinoma by 16-section CT during the arterial phase. They found a very rare case of a LIPA arising from the splenic artery. This type of LIPA origin has not been presented in other investigations.

LIPA and RIPA branching from by a common trunk have significantly less varied types. All authors presented in Table 1 agree that the most common type of such origin is from

the abdominal aorta. Therefore, this trait is definitely well established in the human population.

According to Kimura et al.(17), Basile et al.(3), and Gürse et al.(7), RIPA branching from the abdominal aorta is the most common type of origin of this artery. These studies are in line with the classical anatomical pattern. However, according to Greig et al.(6), Loukas et al.(21), and Aslaner et al.(2), the RIPA arises much more frequently from the celiac trunk. In our opinion, more investigations are necessary to determine whether the current anatomical pattern should be changed.

Interestingly, the most common type of LIPA origin according to Greig et al.(6), Loukas et al.(21), Basile et al.(3), and Aslaner et al.(2) is a branch from the celiac trunk. This is not line with the accepted anatomical pattern, which assumes that both the LIPA and RIPA arise most frequently from the abdominal aorta. The study by Gürse et al.(7) is the only one that confirmedthe classical pattern accepted by medical universities, raisingthe question of whether it should be changed.

The foregoing tables present the frequency of occurrence of IPAs arising from various arterial vessels. However, we propose our own classification of IPA origins based on the available literature (Table 4). The most important feature of our classification is the presentation of complex correlations in a simple, easy-to-remember way. This system focuses on the location of origin only. We do not include the frequency, side of the body, or kind of branching (by a common trunk or direct). Therefore, it is more readable and potentially valuable in the clinical setting, where knowledge of the origins of various arteries is crucial for surgical or radiological procedures.

Relationship between origin of IPA and aorta

The above tables present the frequency of IPAs arising from the aorta. However, the exact location in relation to the aorta is not shown; these arteries can branch off from it at different levels or sides. Several researchers have described this type of IPA origin more precisely(3, 17, 35). Basile et al.(3) found cases of the RIPA and LIPA originating via a common trunk from the aorta at the left side of the celiac trunk (12%) or from the middle ventral aortic wall above the origin of the celiac trunk (9%). Kimura et al.(17) distinguished three classes ofRIPA branches from the aorta: supraceliac (32%), between the celiac trunk and

superior mesenteric artery (17%), and between the superior mesenteric and right renal arteries (8%). So et al.(35) also examined RIPA origin sites and offered more precise descriptions. They distinguished five origin types: supraceliac (20.5%), juxtaceliac(11.7%), between the celiac trunk and superior mesenteric artery (12.3%), juxta-SMA (7.9%), and suprarenal (5.5%).

Branches of the inferior phrenic artery

IPAs give off several branches and arteries that supply other structures(2, 6, 21, 22, 37):

- superior adrenal artery – this vessel is one of three arteries that supply the suprarenal gland, which is known for its rich vascularity. The other two are the inferior adrenal and middle adrenal arteries, branching from the renal artery and aorta respectively.
- branches to the spleen
- branches to the liver
- branches to the stomach
- branches to the esophagus
- branches to the inferior vena cava
- branches to the retroperitoneum
- branches to the kidney and renal capsule

It has also been reported that IPAscangives off aberrant vessels:

- accessory left gastric artery – Heymann et al.(11) presented five cases of such abnormalities as revealed by angiography. In these patients, a conventional left gastric artery arose from the celiac trunk, but each patient had an additional vessel supplying the gastric fundus.The frequency of an accessory gastric artery is unknown. However, its appearance can be significant in surgical procedures involving the gastric fundus; for example,in bariatric embolization and angiography for upper gastrointestinal bleeding.
- dorsal pancreatic artery –this vessel supplies blood to the dorsal part of the pancreatic body. It is divided into two branches. The right branch creates anastomoses with branches

from the gastroduodenal artery. The left branch (called the transverse pancreatic artery) anastomoses with the great pancreatic artery. A dorsal pancreatic artery arising from the splenic artery is the most common anatomical pattern. However, Hagiwara et al.(9) presented a case in which this artery branched from the IPA; it was noted during transarterial chemoembolization and subsequently confirmed by computed tomography.

- accessory inferior phrenic arteries

Several studies have characterized the ascending and posterior branches of the LIPA, which can arise from various sources as independent arteries(7,8). Gürse et al.(8) presented an interesting case in which the ascending branch of the LIPA originated from the celiac trunk and the posterior branch from the aorta. According to their statistical analysis, this variant occurs in 3.85% of cases. The same vascular variant was previously reported by Kim et al. (16).

A rare case of accessory phrenic arteries was described by Zeng et al.(38). In a 69-year-old male, interventional radiography revealed a LIPA supplying the lesser curvature of the stomach and a right accessory phrenic artery conveying blood to the duodenum. Such variants of the gastrointestinal vascular system are significant in the planning of upper abdominal surgery.

Diagnostics

Effective surgical intervention for vascular disease depends on accurate diagnosis and identification of the location and type of lesion(26).Owing to the variable anatomy of the IPA, preoperative diagnosis is very helpful in planning surgical procedures and thus optimizing treatment outcomes(3).

A method that is currently widely used in the diagnosis of vascular pathology is magnetic resonance angiography(24).It is gaining popularity because it is a safer and non-invasive alternative to digital X-ray angiography(14). In addition, this technique avoids ionizing radiation and employs a contrast agent that is not nephrotoxic and is much less frequently associated with allergic reactions(12). MRA can be used with a variety of techniques. In particular, we distinguish between techniques that require contrast and those that do not(24). One technique that does not use contrast is balanced steady-state free precession (bSSFP), which is a method of visualization aneurysms. Imaging with this

procedure allows differentiation of blood in the vessel lumen and thrombus. However, contrast-enhanced magnetic resonance angiography (CE-MRA) is a more precise and reproducible technique that can be performed in seconds with relatively few artifacts, especially in comparison to non-contrast techniques(24). Dynamic magnetic resonance (MR) imaging using three-dimensional (3D) gradient-echo (GRE) with fat-suppression has become important in abdominal MR studies. Thin-segmented, multiphase, three-dimensional contrast-enhanced dynamic MR sequences with fat suppression are potentially useful for imaging small abdominal vessels such as the IPAs(13). These are clinically relevant because, for example, they can be a source of bleeding resulting from trauma or can be the vessels supplying hepatocellular carcinoma (HCC). Fat suppression is essential for evaluating small IPAs because high signals from fat and chemical shift artifacts impair the visualization of these vessels. Fat suppression by increasing the contrast between enhanced vessels and low-signal fat can improve the visualization of IPAs(13).

Computed tomography angiography (CTA) is another important tool in vascular imaging. Furthermore, it is also employed to detect complications after treatment, such as thrombosis or internal leakage after aneurysm repair(18). CTA is a quick diagnostic imaging procedure that produces images of blood vessels after injecting a contrast agent and using X-rays. Two-dimensional (2D) and three-dimensional (3D) visualization methods are routinely used in CTA to obtain images comparable to those obtained via catheter angiography. There are also several post-processing methods that include multiplanar reconstruction (MPR), maximum intensity projection (MIP), curved planar reconstruction (CPR), and volume rendering (VR).MRP produces images in arbitrary planes, resulting in quantitative analysis of both the lumen and the vessel wall. However, it can only generate 2D images(20). CPR is also a two-dimensional image, displaying a cross-section of the vessel along its entire length, which is clearly visualized(31). VR images preserve the original anatomical spatial relationships and have a 3D appearance, so vascular interrelationships can be visualized. In contrast, MIP is valuable as an additional display, especially for imaging smaller vessels(29). Noninvasive vascular imaging by CT angiography has become an increasingly relevant diagnostic technique. Multidetector computed tomography (MDCTA) is a quick and precise method for vascular anatomical assessment and diagnosis of vascular abnormalities(15). This technique allows the anatomy of the IPA to be assessed in a relatively short time, which can be valuable in planning embolization treatment sessions(3). Specific advantages of MDCTA vascular imaging include more accurate visualization of details, including stenoses and the

presence and location of vascular anomalies. In addition, MIP rendering is valuable as an additional display, especially when smaller vessels are imaged (29). MDCTA can reveal the real sizes of lesions such as aneurysms, thrombi, or arterial ruptures. Advances in MDCTA technology have contributed significantly to diagnosis and treatment planning in vascular disease(15). Owing to the variable anatomy of the IPA, preoperative diagnostic MDCTA is very helpful in planning surgical procedures. This technique is also significant in imaging the different variants of the IPA, which helps in selective catheterization of the vessel and eliminates the need for repeated contrast injections and angiograms in different projections(3).

Clinical relevance

It has been reported in the literature that IPAs are involved in several disorders and pathologic conditions. We reviewed the role of these arteries in diseases and clinical management below.

IPAs are the main vessels supplying the diaphragm. In addition, they constitute extrahepatic collateral arterial pathways that supply hepatic malignancies. The RIPA and LIPA constitute more than half of the collaterals involved in forming the arterial pathways supplying hepatic malignancies, the RIPA being the more common(7). It has been estimated that RIPA is involved in 70 – 83% of extrahepatic arteries supplying hepatocellular carcinoma. Because it runs in direct contact with the bare area of the liver, the RIPA can form anastomoses with intrahepatic arteries. This facilitates the blood supply from the extrahepatic arteries to hepatic lesions when the natural tumor supply is impaired(23). Apart from being an important extrahepatic artery for tumors of the liver, especially those located in the uncovered part of this organ, IPA also provides the essential blood supply to lung metastases(39).

Branches of the LIPA supply blood to the stomach and esophagus and can also be involved in arterial bleeding at the esophagus-gastric junction and Mallory-Weiss tears(7, 27, 34).

The LIPA can also be involved in atherosclerotic ischemic heart disease, anastomosing with trans-diaphragmatic collaterals, and the left anterior descending coronary artery. This anastomosis arises from a connection between the LIPA and pericardiophrenic musculophrenic arteries(2).

The development of IPA pseudoaneurysm also has been described in the literature(19, 25, 32). Such disorders are a consequence of partial or complete rupture of the vessel wall, leading to hemorrhage(28). It is worth emphasizing that IPAs can be responsible for hemoperitoneum or hemothorax as a result of their pseudoaneurysm rupture(10, 19).

The IPA can also have a role in diaphragm injury. A very rare case of diaphragmatic rupture during cardiopulmonary resuscitation (CPR) has been reported. Digital subtraction angiography revealed active bleeding from a branch of the RIPA. Thus, it is important to recognize the possibility that organs such as the diaphragm can be injured during energetic CPR(30).

The IPAs can also have a major role in diaphragmatic hernia repair, especially when rare anatomical defects or abnormal-looking vessels are involved. Calin et al.(4) described a rare case of diaphragmatic hernia in which an abnormally-sized LIPA presented a challenge to surgery. Knowledge of IPA variants is also necessary for treating surgical and traumatic vessel injuries and hemoptysis, especially when caused by pulmonary pathologies. However, when the arteries of vital organs are stenosed, the IPAs are key to preventing the development of ischemia in those organs(2).

CONLUSIONS

The IPA has the ability to form rich collaterals with other arteries located in the thoracic and abdominal cavities. Thanks to this, it has an important role in pathological processes, the most common of which is supplying hepatic malignances. Moreover, the IPA can become a pathway of lung metastasis. IPA injuries almost always result in life-threatening bleeding. On the other hand, this arterial vessel has great potential for protecting vital organs when their main arteries are stenosed. The present study demonstrates that knowledge of the anatomy of human blood vessels is helpful for better understanding of physiological and pathophysiological processes.

Ethical approval and consent to participate

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Table 1. Types of RIPA and LIPA origin by a common trunk

Types of origin	Greig et al. (%) 1951	Loukas et al. (%) 2005	Kimura et al. (%) 2007	Basile et al. (%) 2008	Gürse et al. (%) 2015	Aslaner et al. (%) 2017	Szewczyk et al. (%) 2020
Abdominal aorta	18.1	31	21	21	11.53	16.4	6.24
Celiac trunk	12.1	11	9	16	7.69	12.6	-
Right renal artery	-	-	-	-	-	0.4	-
Left gastric artery	0.7	-	-	-	-	0.1	-
Types of origin	Greig et al. (%) 1951	Loukas et al. (%) 2005	Kimura et al. (%) 2007	Basile et al. (%) 2008	Gürse et al. (%) 2015	Aslaner et al. (%) 2017	Szewczyk et al. (%) 2020
Abdominal aorta	18.1	31	21	21	11.53	16.4	6.24
Celiac trunk	12.1	11	9	16	7.69	12.6	-
Right renal artery	-	-	-	-	-	0.4	-
Left gastric artery	0.7	-	-	-	-	0.1	-
Types of origin	Greig et al. (%) 1951	Loukas et al. (%) 2005	Kimura et al. (%) 2007	Basile et al. (%) 2008	Gürse et al. (%) 2015	Aslaner et al. (%) 2017	Szewczyk et al. (%) 2020
Abdominal aorta	18.1	31	21	21	11.53	16.4	6.24
Celiac trunk	12.1	11	9	16	7.69	12.6	-
Right renal artery	-	-	-	-	-	0.4	-
Left gastric artery	0.7	-	-	-	-	0.1	-

Table 2. Types of separate origin of RIPA (without common trunk)

Types of origin	Greig et al. (%) 1951	Loukas et al. (%) 2005	Kimura et. al. (%) 2007	Basile et al. (%) 2008	Gürse et al. (%) 2015	Aslaner et al. (%) 2017
Abdominal aorta	28	30.67	36	28	50	25.2
Celiac trunk	29.2	36	20.79	25	3.85	30.7
Right renal artery	-	17	11	5.5	7.69	10.4
Left gastric artery	1.9	3	2	4	3.85	4.1
Common hepatic artery	-	-	-	-	-	0.1
Accessory right hepatic artery	0.2	-	-	-	-	-
Spermatic artery	0.2	-	-	-	-	-
Dorsal pancreatic artery	-	-	1	-	-	-
Proper hepatic artery	-	2	-	0.5	-	-

Table 3. Types of separate origin of LIPA (without common trunk)

Types of origin	Greig et al. (%) 1951	Loukas et al. (%) 2005	Basile et al. (%) 2008	Gürse et al. (%) 2015	Aslaner et al. (%) 2017
Abdominal aorta	25,9	37,67	26,5	34,61	25,2
Celiac trunk	40	43	28	23,07	40,3
Left gastric artery	1,9	2	-	-	2,4
Left renal artery	-	5	1	-	2
Left hepatic artery	-	-	-	-	0,5
Right renal artery	-	-	-	-	0,1
Accessory left hepatic artery	0,2	-	-	-	-
Proper hepatic artery	-	1	-	-	-
Splenic artery	-	-	1	-	-

Table 4. New classification system based on the available literature proposed by Marcinkowska et al.

*this type contains blood vessels that are the main arterial supply to the liver

**this type includes the celiac trunk and its branches without the common hepatic arteries, which are included in type I

Type	Description
I	Hepatic arteries*
	A–common hepatic artery
	B – proper hepatic artery
	C – left hepatic artery
	D – accessory left hepatic artery
	E – accessory right hepatic artery
II	Coeliac trunk and its branches**
	A – coeliac trunk
	B – left gastric artery
	C – splenic artery
III	Renal arteries
	A – right renal artery
	B – left renal artery
IV	Abdominal aorta
V	Dorsal pancreatic artery
VI	Spermatic artery

Figure 1. a) Right inferior phrenic artery(RIPA) and left inferior phrenic artery(LIPA) origin by a common trunk from the abdominal aorta. b) Right inferior phrenic artery(RIPA) and left inferior phrenic artery(LIPA) origin by a common trunk from celiac artery c) Right inferior phrenic artery(RIPA) and left inferior phrenic artery(LIPA) origin by a common trunk from right renal artery d) Right inferior phrenic artery(RIPA) and left inferior phrenic artery(LIPA) origin by a common trunk from the left gastric artery.

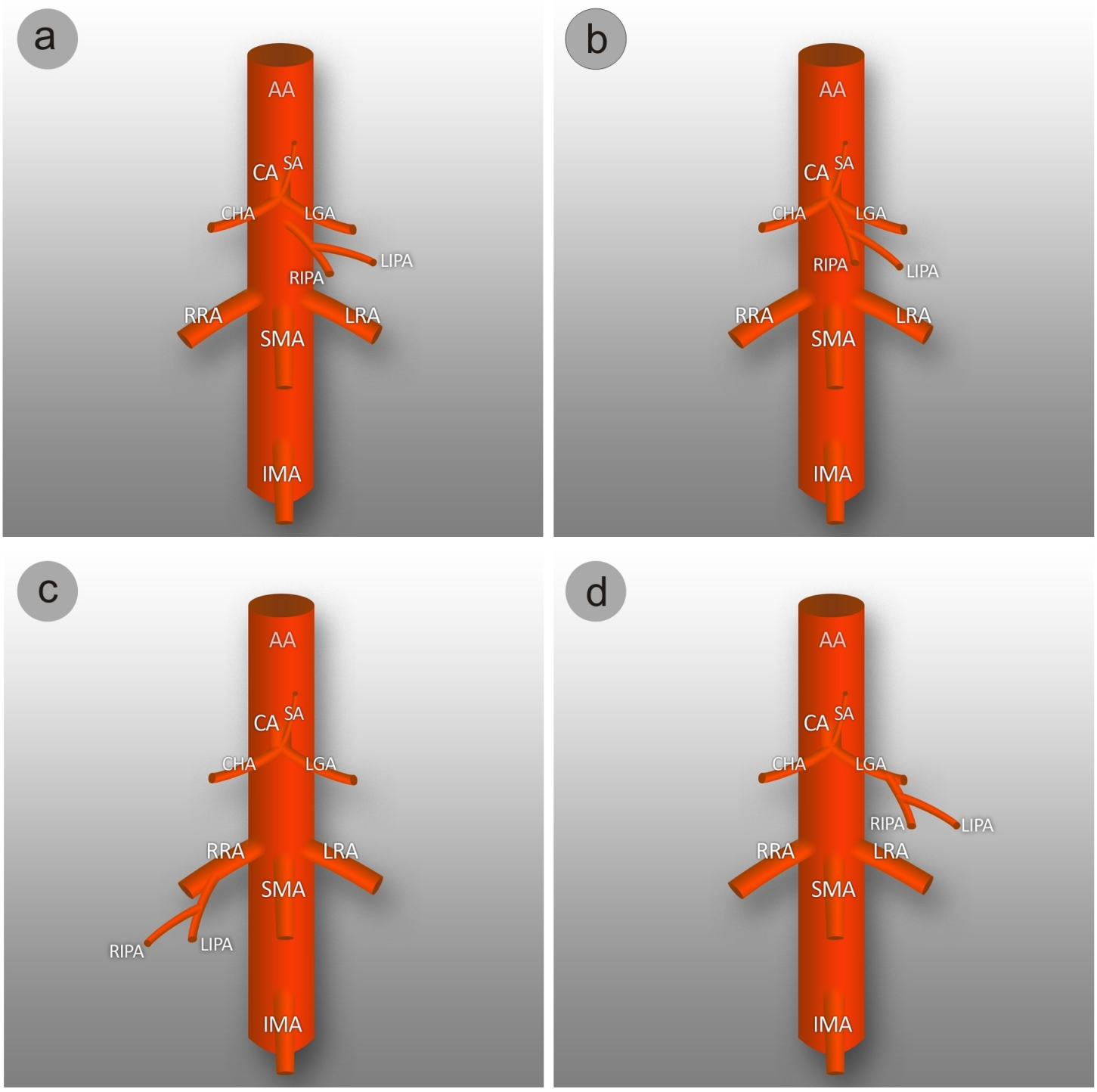
Figure 2. a) Right inferior phrenic artery(RIPA) (without common trunk) from abdominal aorta b) Right inferior phrenic artery(RIPA) (without common trunk) from celiac trunk c) Right inferior phrenic artery(RIPA) (without common trunk) from right renal artery d) Right inferior phrenic artery(RIPA) (without common trunk) from the left gastric artery.

Figure 3. a) Right inferior phrenic artery(RIPA) (without common trunk) from common hepatic artery b) Right inferior phrenic artery(RIPA) (without common trunk) from accessory right hepatic artery c) Right inferior phrenic artery(RIPA) (without common trunk) from spermatic artery d) Right inferior phrenic artery(RIPA) (without common trunk) from the dorsal pancreatic artery.

Figure 4. a) Right inferior phrenic artery(RIPA) (without common trunk) from proper hepatic artery b) Left inferior phrenic artery(LIPA) (without common trunk) from abdominal aorta c) Left inferior phrenic artery(LIPA) (without common trunk) from celiac trunk d) Left inferior phrenic artery(LIPA) (without common trunk) from the left gastric artery.

Figure 5. a) Left inferior phrenic artery(LIPA) (without common trunk) from left renal artery b) Left inferior phrenic artery(LIPA) (without common trunk) from left hepatic artery c) Left inferior phrenic artery(LIPA) (without common trunk) from right renal artery d) Left inferior phrenic artery(LIPA) (without common trunk) from accessory left hepatic artery.

Figure 6. a) Left inferior phrenic artery(LIPA) (without common trunk) from proper hepatic artery b) Left inferior phrenic artery(LIPA) (without common trunk) from splenic artery d)Accessory inferior phrenic artery from the inferior phrenic artery.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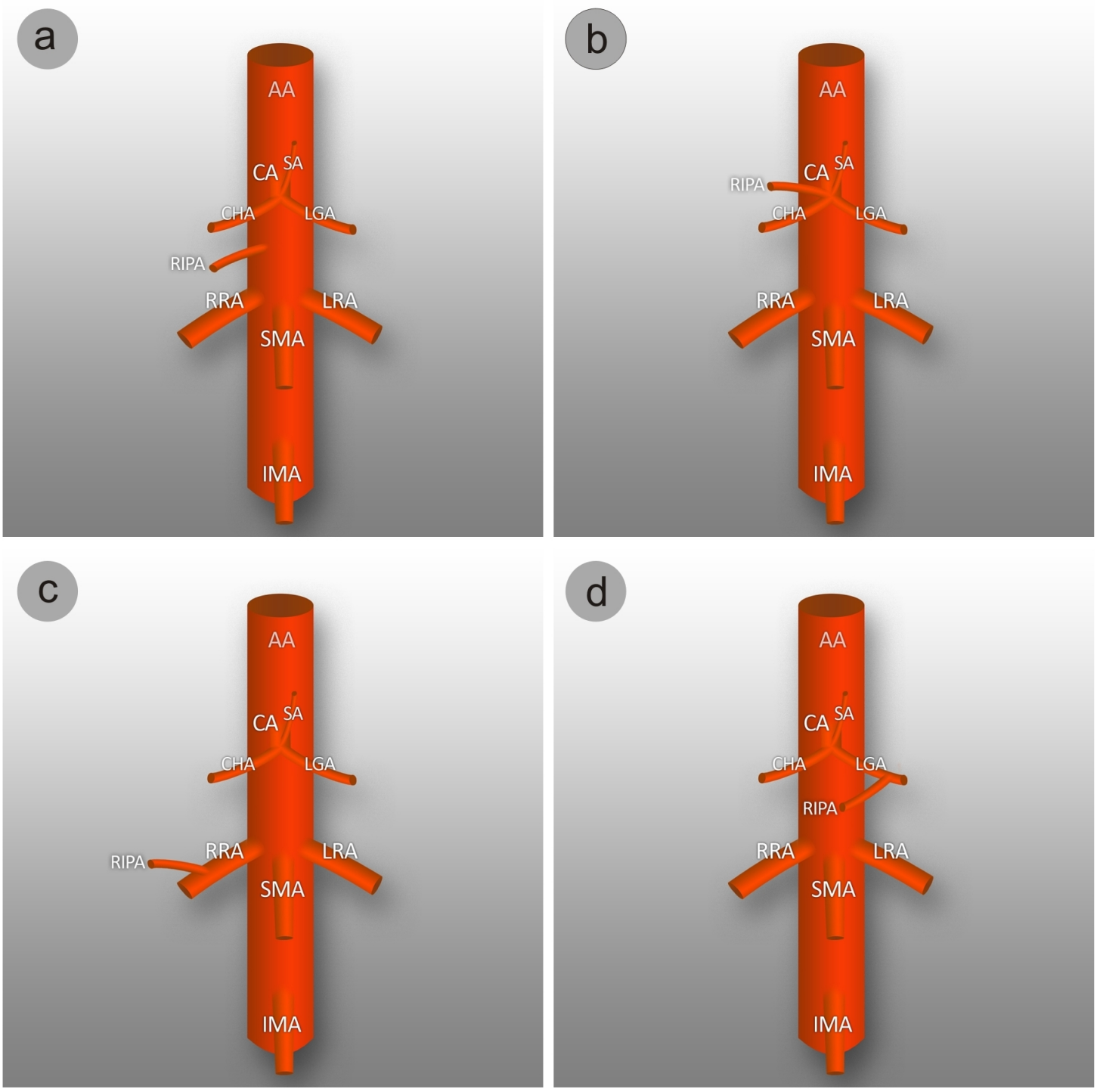
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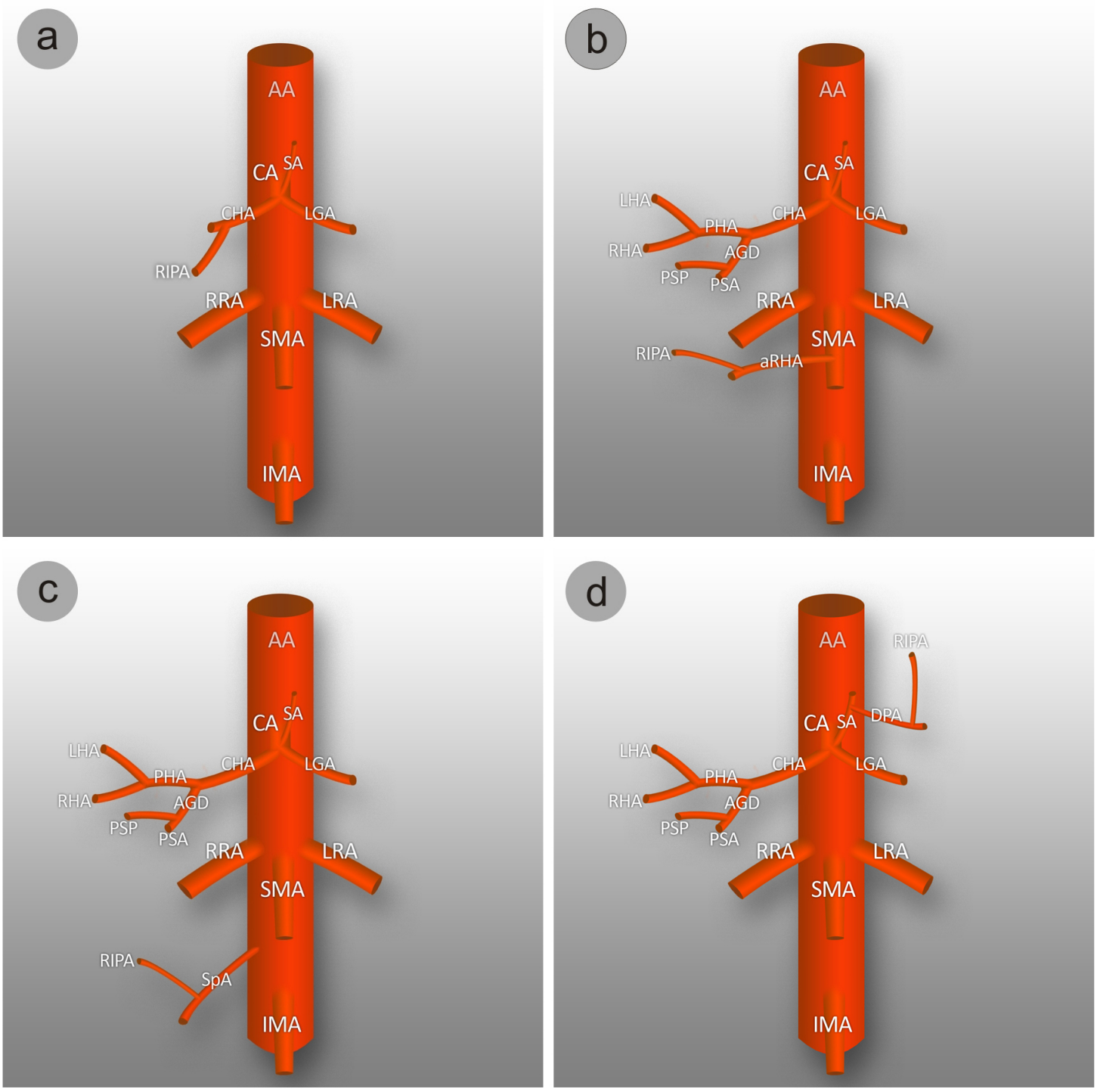
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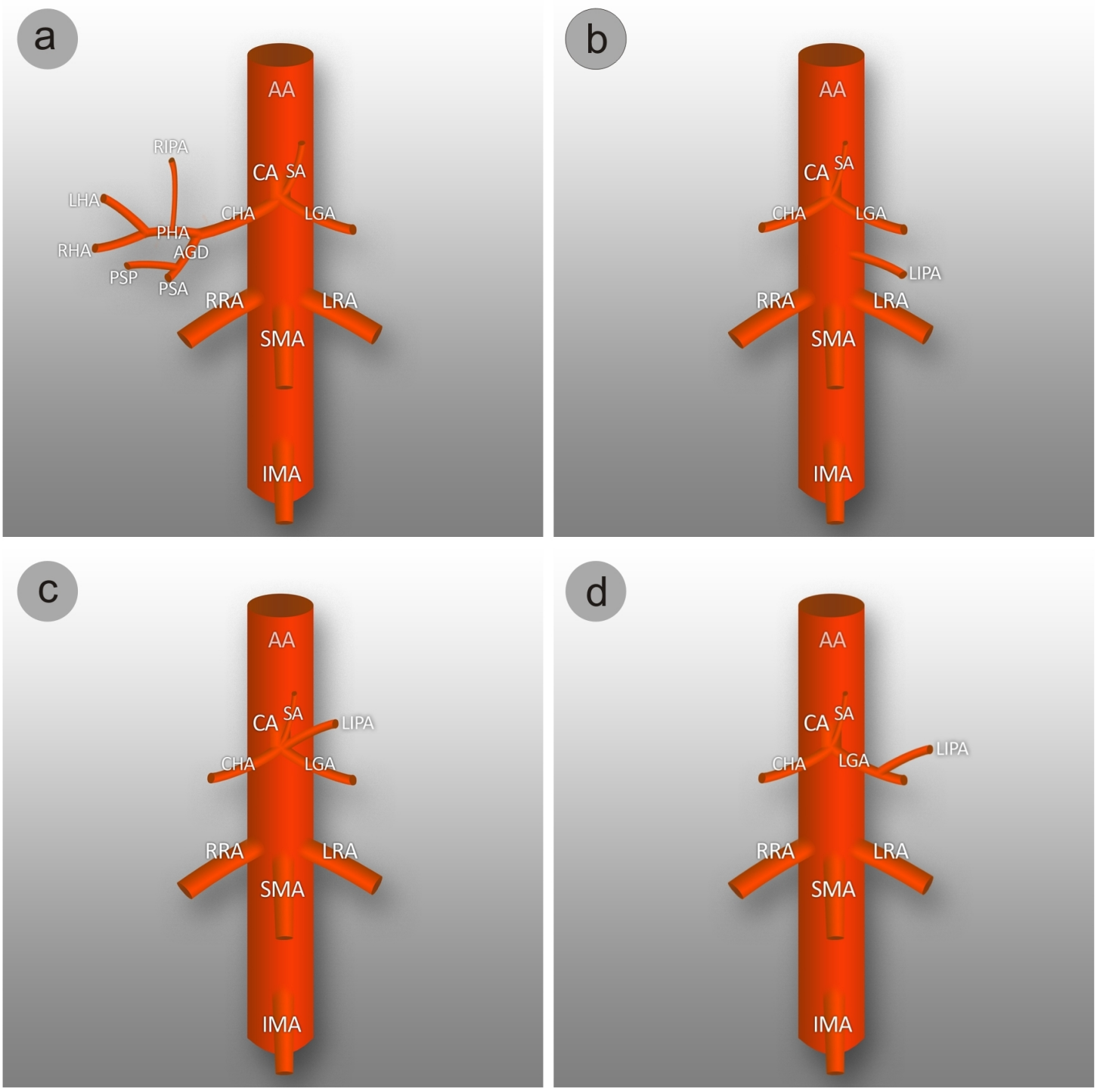
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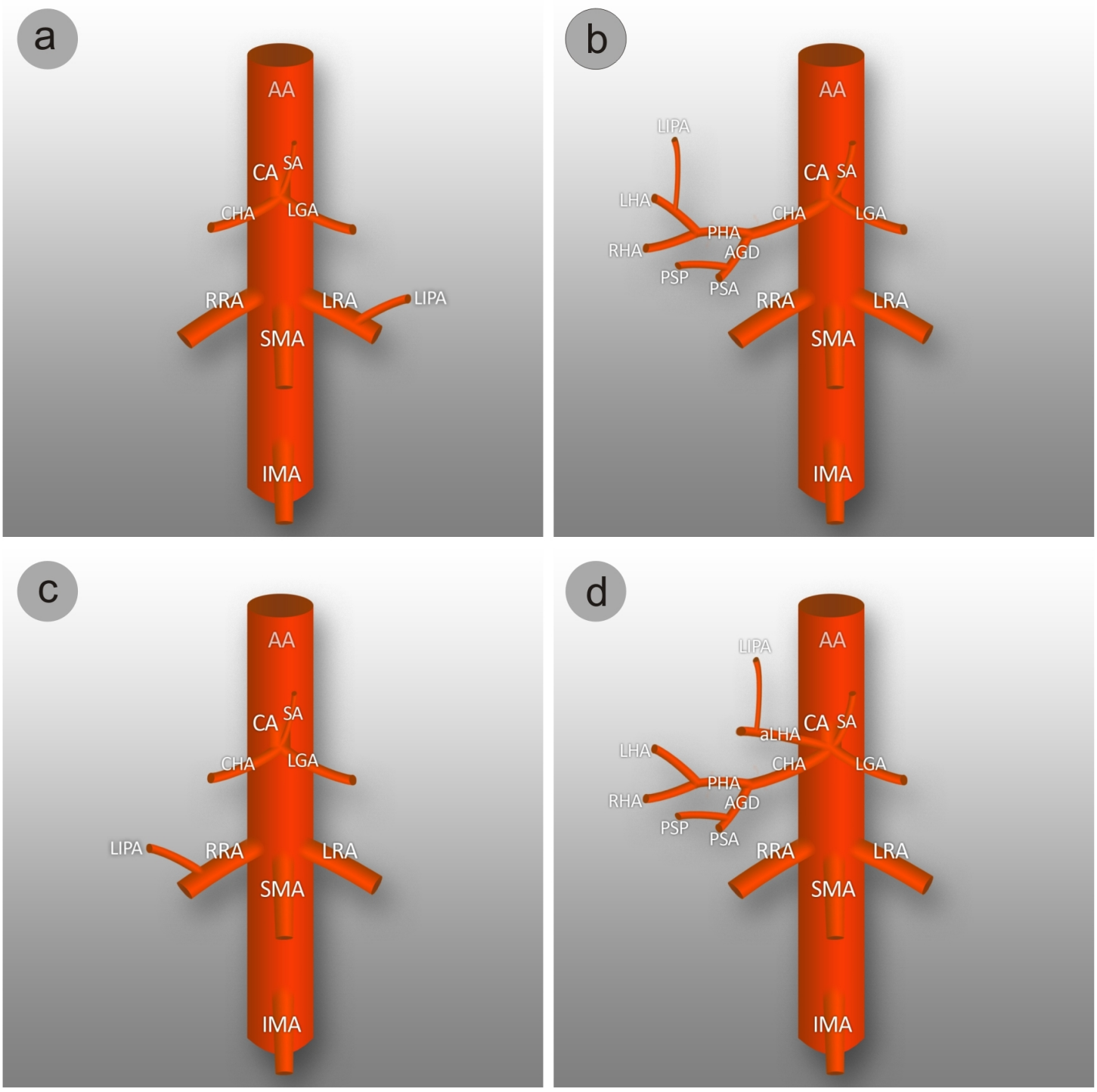
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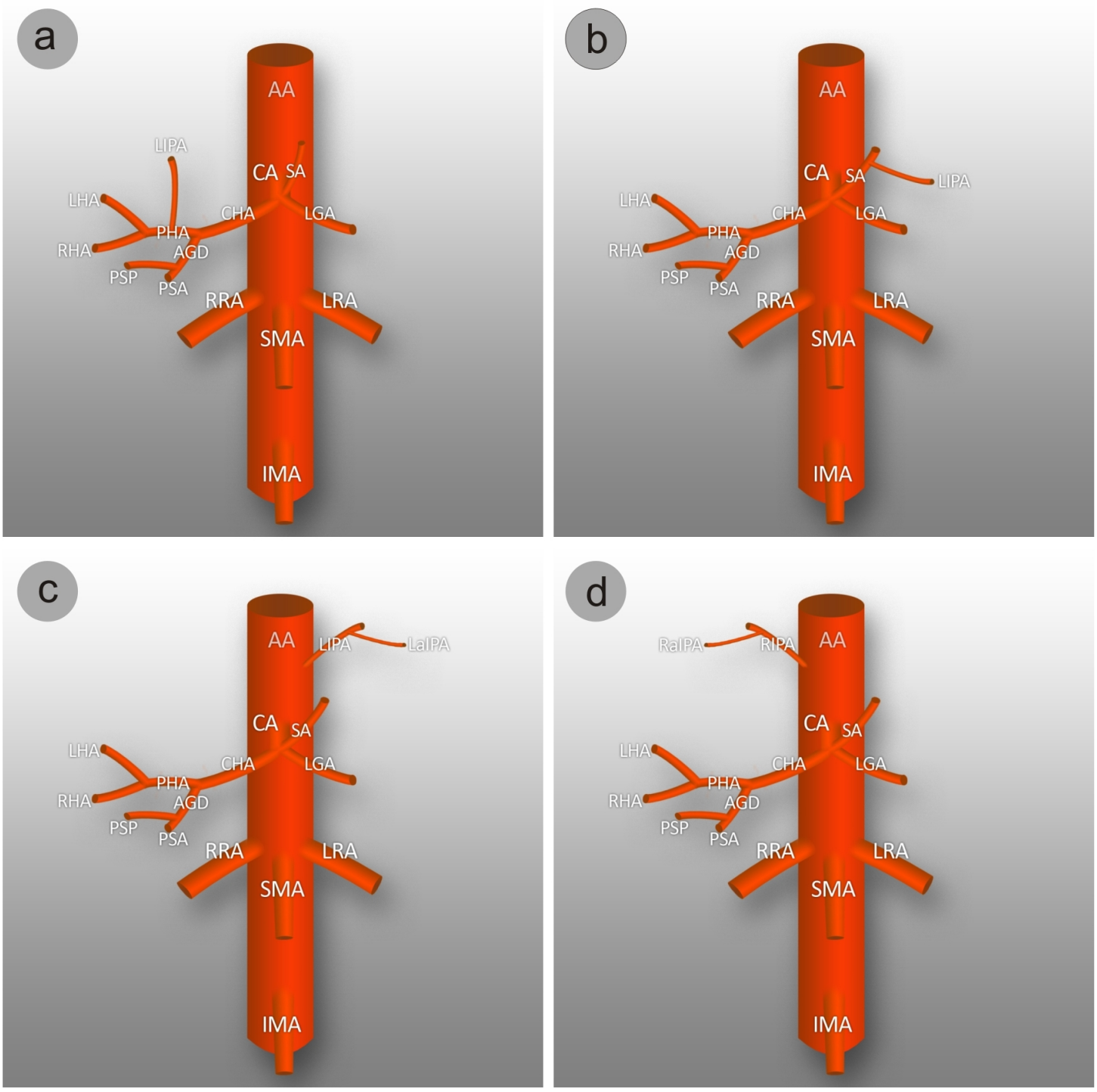
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