Arcuate Foramen of the Atlas Vertebra and its Correlation with Clinical Implications in the Craniocervical Region: A Systematic Review and Meta-analysis

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Key words
- Arcuale foramen
- Arcuate foramen
- Clinical symptoms
- Craniocervical region
- Foramen arcuate atlantis
- Kimmerle anomaly
- Pons posticus
- Ponticulus posticus
- Posterior ponticle
- Retroarticular superior foramen
- Vertebral artery

Abbreviations and Acronyms
CT: Computed tomography
ESP: Elongated Styloid Process
DD: Donor dissection
Rx: x-Ray
PP: Ponticulus posticus (arcuate foramen)

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BACKGROUND CONTEXT: **The arcuate foramen (FA) can present in various forms: it may be complete, incomplete, unilateral, or bilateral. This anatomical feature is relatively common, occurring in approximately 3%—15% of the population, with a higher prevalence in females.**

PURPOSE: **The purpose of this study is to provide rigorous scientific evidence detailing the anatomical characteristics of the AF. Furthermore, this work aims to analyze the prevalence and explore its relevance in clinical applications and surgical procedures.**

STUDY DESING: **Systematic review and meta-analysis.**

METHODS: **Data were compiled from numerous published studies accessed from the databases Medline, Scopus, Web of Science, EMBASE, Google Scholar, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and of April 2025. Methodological quality was evaluated with an assurance tool for anatomical studies (AQUA). Pooled prevalence was estimated using a random effects model, and differences in FA variant rates were assessed.**

RESULTS: **FA variants were identified, the data were categorized into 3 groups: the first category was the type of sample, divided into cadaver donor samples and imaging findings; the second analysis focused on the geographical region from which the sample originated; and finally, sex and laterality were also considered. Overall, the prevalence of these variations was 16% (CI: 11%—20%), and significant heterogeneity (98.8%) was observed. Significantly higher rates were observed in the following subgroups: imaging studies versus donor data ($P = 0.032$), right side versus left side ($P = 0.034$), and bilateral versus unilateral findings ($P = 0.019$). Among the concerns raised were studies on the risk of iatrogenic damage during surgical procedures. Several studies also indicated a higher frequency of vertebral artery variations in patients with symptoms such as recurrent headaches, vertigo, dizziness, and/or syncope.**

CONCLUSIONS: **This review emphasized the importance of considering the vertebral artery (VA) in the preoperative assessment of surgical procedures involving the placement of screws in the cervical spine, such as treatment for atlantoaxial instability. Lack of knowledge regarding the anatomy of this region can lead to complications, such as vertebral artery injury and, consequently, impaired blood flow to the brain, cerebellum, and brainstem. Therefore, the authors recommend further research on this topic, particularly in other patient populations and in collaboration with other disciplines, to advance our understanding of the vertebral artery and to provide valuable tools for healthcare professionals and researchers, thus contributing to improved patient care.**

INTRODUCTION

The arcuate foramen (AF) also known as ponticulus posticus or kimmerle anomaly, pons posticus, posterior ponticle, or retroarticular superior foramen is an anatomical variant found in the posterior arch of the atlas or C1 vertebra due the calcification of the lateral border of the posterior atlanto-occipital membrane (Table 1). As a result, the atlantic portion (V3) of the vertebral artery (VA), the suboccipital nerve, and the cervical venous plexus can pass through this created foramen. The foramen can be complete, incomplete, unilateral, or bilateral.[1-3]

While the etiology of the AF is undetermined, the embryology of the atlas has been extensively documented in the literature.[4] Beginning in the seventh week of intrauterine life, the posterior arch and lateral masses of the atlas begin to ossify, with a progressive ossification dorsally and an ossification center in each lateral mass.[5] At 4 years of age, the final fusion takes place. The occurrence of a complete or incomplete foramen has been explained by a variety of theories. The VA groove is located behind the lateral masses of the atlas. The late ossification of the posterior atlanto-occipital membrane and the connective tissue around the VA may be the reason.[6] Apart from its embryological etiology, there are different explanations for the AF that have been proposed related to genetic factors, congenital malformations, calcification of the ligament associated with aging, the pulsation of the VA itself or even external mechanical factors, such as trauma or bad posture.[7] The prevalence of this anatomic variant significantly correlates with geographic location, but it has been reported that it presents in 5.14%–37.83% of cases in the occidental[1] population, where it is more common.[3,8] The AF is usually observable on a head and neck lateral plain film radiograph of the craniocervical junction. This form of imaging, however, is unable to differentiate if the AF is unilateral or bilateral. Other imaging techniques, such as computed tomography (CT), allow for this visualization.[7]

There are different ways to classify the presence of the AF: complete or incomplete ossification of the ligament to more specific classifications. One of the most thorough and detailed classification is the one proposed by Hasan et al.[9] This classification divides the AF into 6 subgroups. These subgroups are based on the characteristics of the posterior arch presented for VA passage. In class I, the posterior arch presents an impression of the VA. In class II, the posterior arch also has an impression of the VA, but it is much more profound. In class III, the AF partially presents with a bony spicule shape. In class IV, the AF is complete. In class V, a lateral bridge extends from the lateral mass of the atlas to the transverse apophysis. Finally, in class VI, the posterior arch presents a posterolateral tunnel that is much more extensive than the previous classes.[9]

The clinical relevance of the AF is that although its presence is usually asymptomatic, in 5.5%–7% of cases report that when the neck is rotated or lateral flexed, signs and symptoms of verterbro-basilar insufficiency manifest.[10] Symptoms include cervicogenic migraines, neurosensorial auditory loss, vertigo, neck, shoulder and arm pain, or even loss of the postural muscle tone and consciousness. They can often be misdiagnosed due to their similarity with other conditions.[11] AF has also been related to Barré-Liéou syndrome, which includes signs and symptoms such as retroocular pain, recurrent alterations in vision, deglutition and phonation due disruption of the blood flow, apart from headaches and vasomotor alterations in the face.[10-13]

The study of AF is also relevant with regard to spine interventions at the cervical level, specifically in orthopedic or neurosurgical procedures that involve the use of screws. For example, in the treatment for atlantoaxial instability, lack of knowledge that a patient has an AF can result in the performing surgeon believing that the posterior arch of the patient is thicker than it is when seen in a dorsal view, causing the surgeon to utilize screws with an inadequate caliber for the case, compromising the VA.[14]

In this revision by a meta-analysis, we analyzed AF prevalence, with the intent of

Table 1. Names for Arcuate Foramen

Search Terms Used in the Literature Database
Arcuate foramen (*Latin*)
Arcus atlantis ossificatus (ossified bridge variant-*Latin*)
Atlas bridging
Atlas bridging in hominidis (paleoanthropolgy)
Canalis arteriae vertebralis (*Latin*)
Dorsal ponticle
Foramen arcuale atlantis (*Latin*)
Foramen arcuale (*Latin*)
Foramen atlantoideum (*Latin*)
Foramen atlantoideum posterius/vertebrale (*Latin*)
Foramen processus transversi atlantis (*Latin*)
Foramen retroarticular (*Latin*)
Foramen retroarticulare superior (*Latin*)
Ponticulus arteriae vertebralis (*Latin*)
Pons posticus (*Latin*)
Oblique atlanto-occipital ligament
Kimmerle variant
Kimmerle deformity
Kimmerle anomaly
Foramen sagittale (*Latin*)
Ponticulus posticus (*Latin*)
Ponticulus posterior (ponticulus posticus) of the atlas
Posterior atlantoid foramen
Posterior glenoid process
Posterior glenoid spiculum
Posterior ponticlelimitation
Retroarticular canal of the atlas
Retroarticular ring
Retroarticular vertebral artery ring
Retrocondylar bony foramen
Spiculum (*Latin*)

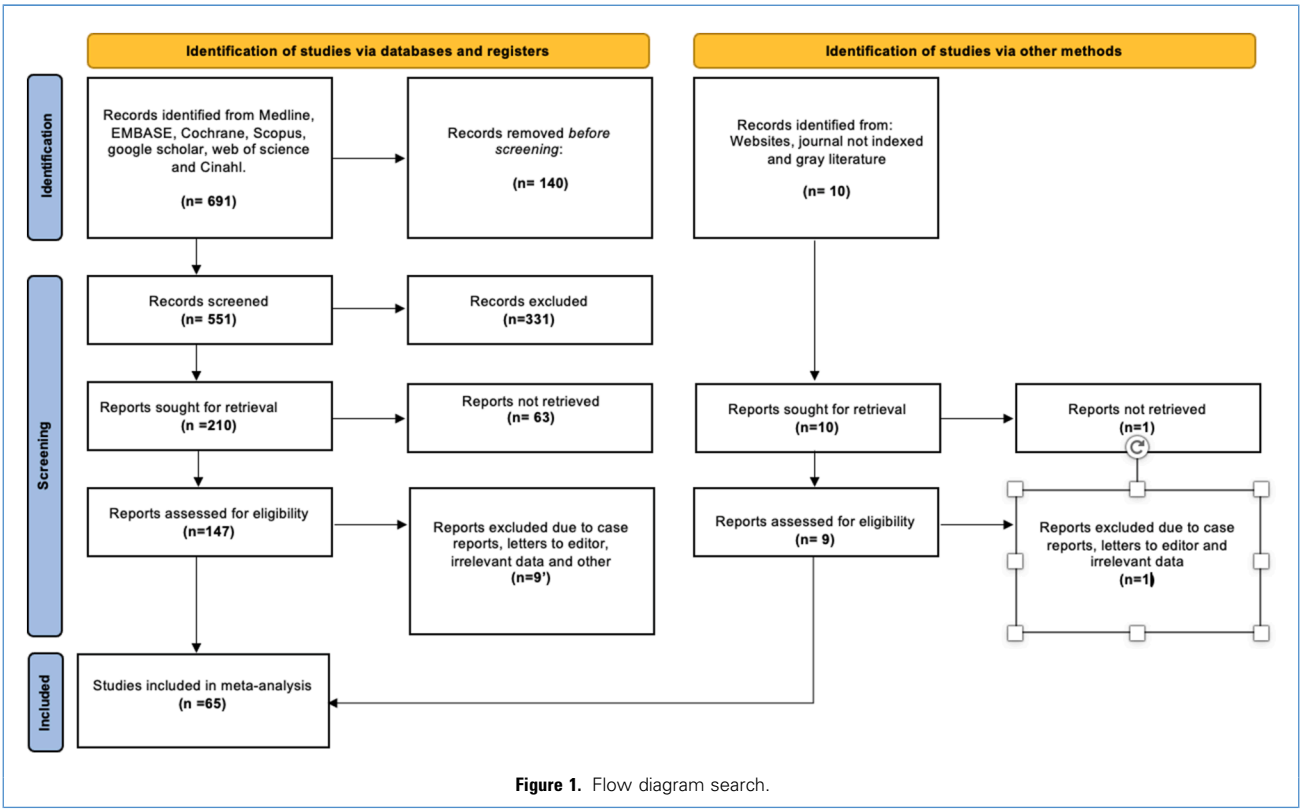

Figure 1. Flow diagram search.

gaining a better understanding about the way it presents in the population, adding visibility to its clinical and surgical implications.

METHODS

Protocol and Registration

The PRISMA 2020 statement guided the systematic review.[15] The registration number in the Systematic Reviews Registry (PROSPERO) is CRD420250650960.

Electronic Search

In January 2025, we searched several online databases to ensure we included the most relevant studies for our research question. These databases included MEDLINE (via PubMed), Google Scholar, Web of Science (WOS), EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Scopus, covering publications from their inception until April 2025. Our search strategy involved combining the following terms: *"arcuate foramen" (not MeSH)*, *"ponticulus posticus" (not MeSH)*, *"variations atlas" (not MeSH)*, *"anatomical variations" (not MeSH)*, *"clinical anatomy" (not MeSH)*, *and "aberrant anatomy" (not MeSH)*. We utilized the Boolean operators AND, OR, and NOT in this process (**Supplementary Table 1**).

Eligibility Criteria

The present systematic review included studies that examined the association between AF morphological variants and various clinical conditions.[5] To be eligible for inclusion, the studies needed to meet the following criteria: 1) They must have involved dissections or imaging identifying the presence of AF morphological variants; 2) They should report the prevalence of subjects with gastric vein variants and their correlation with craniocervical pathologies; 3) Only research articles were considered, including retrospective and prospective observational studies, published in English in peer-reviewed journals and indexed in the relevant databases. As exclusion criteria, we used the following criteria to eliminate studies from our selection: 1) Sample: studies carried out in animals; 2) Studies that analyzed variants of the region or system outside the hepatic region or its drainage area or tract; and 3) Studies including letters to the editor or comments or case reports.

Study Selection

Three authors conducted thorough independent analyses to select studies. Two authors (Cornejo J and Martinez J) initially reviewed the titles and abstracts of references retrieved from the database searches. The full texts of these references were obtained for the studies they deemed

Table 2. Characteristics Included Studies

Author/year	G. Region	Age Mean/Sex	F.I. (Number of Cases/Total of Cases) Prevalence	Symptoms	Evaluation Mode	Type of Variant	Clinical Implications
Agrawal et al. 2012	India	Not documented/Not documented	2/28	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 1 Left: 1	Knowledge of these foramina may be important for orthopedic surgeons, neurologists, neurosurgeons, and anthropologists.
Awadalla and Fetouch 2009	Egypt	Not documented/Not documented	2/76	Not documented	CD	Not documented	Association with risks of damage to the vertebral artery during surgery
Baba et al. 2015	India	10. —70/Female 470 Male 530	80/1000	Not documented	Rx	Not documented	Clinical implication in atlas fixation surgery since it could lead to an injury to the vertebral artery which can cause a hemorrhagic accident, death due to thrombosis, embolism or arterial dissection
Baeesa et al. 2012	Saudi Arabia	49,18/Female 198 Male 255	73/255	Not documented	CT	Arcuate foramen presented as follows: Bilateral: 32 Left: 13 Right: 28	Fixation of the V3 segment of the vertebral artery to the atlas constitutes a significant risk during surgical interventions in this region. Any maneuver involving the superior cortex, mobilization of the V3 segment, or insertion of screws in the posterior arch can compromise vascular integrity, resulting in adverse events such as compression, injury, or arterial thrombosis.
Bayrakdar et al. 2014	Turkey	Not documented/Female 453 Male 277	69/730	Not documented	CT	Not documented	It has been associated with conditions such as vertebrobasilar insufficiency, headaches and neck pain in addition to migraines without aura, acute hearing loss, and chronic tension headaches. It is also related to vertigo, Barré Lieou syndrome, photophobia and headaches due to ischemia. Its surgical implication is also mentioned
Beck et al. 2004	New Zealand	35.8/Female 514 Male 490	115/1004	Not documented	Rx	Not documented	clinical involvement in compression of the vertebral artery, clinical involvement has also been seen in vertigo, Barré Lieou syndrome and migraines. There is also a weak association with epilepsy.

Cakmak et al. 2005*	Turkey	49.5 ± 14.43/Female 284 Male 132	37/476	vertigo, shoulder and arm pain, neck pain, lacrimation and headaches	CD + CT	Arcuate foramen presented as follows (Only C): Bilateral: 1 Left: 3 Right: 3 Not documented by the CT method.	Clinical implication to take into consideration in patients with vertigo, headaches, shoulder, arm and neck pain.
De Carvalho et al. 2009	Brazil	Not documented/Not documented	3/30	Not documented	CD	Arcuate foramen presented as follows**	surgical implication to avoid damage to the vertebral artery
Cederberg et al. 2000	USA	26.6/Female 141 Male 114	29/255	Not documented	Rx	Not documented	possible limitation in the normal mobility of the artery and nerve during flexion and extension of the neck. It could also lead to alterations in blood flow and disruption of the arterial nerve plexus, producing headaches, retro-orbital pain, and visual and vasomotor alterations of the face.
Chavez and Perez 2015	Peru	11.3 ± 4.2/Female 70 Male 93	102/1219	Not documented	Rx	Not documented	Not documented
Chen et al. 2015	Taiwan	49 ± 14.2/Female 265 Male 235	23/500	Not documented	CT	Arcuate foramen presented as follows: Bilateral: 5 Left: 14 Right 4	possible limitation of vertebral artery flow when performing rotation and tilt movements. Furthermore, it has been suggested that this variation confuses surgeons when locating screws in atlantoaxial stabilization surgery, which could cause damage to the vertebral artery.
Chitroda et al. 2013	India	Not documented/Female 234 Male 266	40/500	Orofacial pain, migraines and tension headaches	Rx	Not documented	Implication in atlantoaxial fusion surgery to avoid damage to the vertebral artery which could trigger hemorrhagic events and even death due to thrombosis, embolism or arterial dissection. The presence of this foramen has been linked to Barré-Liéou syndrome, which presents symptoms such as headaches, retro-orbital pain, among others.
Cho 2009	South Korea	45.0 ± 19.65/Female 100 Male 100	16/200	cervical problems	CT	Arcuate foramen presented as follows: Bilateral: 7 Unilateral: 9	Surgical implication in surgeries of the cervical spine, injuries could be caused to the vertebral artery and cause vascular accidents and even death due to thrombosis, embolism or arterial dissection

CT, computed tomography; ESP, Elongated Styloid Process; DD, Donor dissection; Rx: x-Ray; PP, ponticulus posticus (arcuate foramen).
*,** indicates a *P*-value less than 0.05 is considered significant.

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Table 2. Continued

Author/year	G. Region	Age Mean/Sex	F.I. (Number of Cases/Total of Cases) Prevalence	Symptoms	Evaluation Mode	Type of Variant	Clinical Implications
Ebraheim et al. 1996	USA	24—68/Female 22 Male 28	1/50	Not documented	CD	Not documented	Knowing the complete anatomy of the foramen may be helpful in avoiding and minimizing injury to the vertebral artery during a posterior exposure of the atlas.
Elgafy et al., 2014	USA	47.1/Female 49 Male 51	14/100	Not documented	CT	Arcuate foramen presented as follows: Bilateral: 5 Left: 6 Right: 3	Preoperative planning is essential to reduce VA injury during C1-C2 instrumentation. Due to the relatively high prevalence of ponticulus posticus in the present study, variations in arcuate foramen morphology, and the possible simultaneous occurrence of elevated VA and ponticulus posticus, surgical candidates should be meticulously evaluated with a preoperative CT scan to facilitate planning the safest technique for C1-C2 instrumentation.
Farman et al. 1979	South Africa	8. —25/Female 116 Male 104	18/220	Not documented	Rx	Not documented	Not documented
Geist et al., 2014	USA	12.2/Female 305 Male 271	60/576	Not documented	CT	Not documented	Possible compression of the vertebral artery during rotation movements causing vertebrobasilar insufficiency syndrome. Compression of this artery is a cause of Barré-Liéou syndrome. It is mentioned that the removal of this variation can alleviate the symptoms of this syndrome.
Gibelli et al. 2016	Italy	10.6/Female 130 Male 91	17/221	Not documented	Rx	Not documented	This anatomical variation is related to various symptoms in addition to a possible cause of adverse events that occur in cervical spine surgeries.
Gopal et al. 2013	India	Not documented/Not documented	24/300	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 7 Left: 10 Right: 7	Possible aggravation of vertebral artery compressions due to extreme rotation movements. Additionally, the presence of the foramen must be taken into account when surgically manipulating the cervical spine.

Gupta et al. 2013	India	Not documented/Not documented	2/35	Not documented	CD	Not documented	Understanding the anatomical variations of the vertebrae could help reduce complications in fusion surgeries in the cervical spine.
Gupta et al. 2008	India	Not documented/Not documented	3/55	Not documented	CD	Not documented	Possible surgical usefulness to avoid and reduce complications such as damage to the vertebral artery or spinal cord during C1 stabilization surgery
Hasan et al. 2001	India	Not documented/Not documented	12/350	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 3 Left: 5 Right: 4	It is thought that an asymmetry in the vertebra due to the development of these bridges can lead to an imbalance in the load that a person has, leading to a dominance of the muscles on the opposite side of the asymmetry. It is mentioned that the symptoms of vertebrobasilar insufficiency could be alleviated by surgical removal of this foramen.
Hong et al. 2008	South Korea	55.7/Female 567 Mle 446	66/1013	cerebral ischemia, headaches, trauma and spine disease	CT	Not documented	Surgical importance in C1 fusion surgery through the insertion of screws to avoid damage to the vertebral artery and operative complications.
Hwan Kim, et. all. 2007	South Korea	Not documented/Female 274 Male 263	78/537	Not documented	Rx + CT	Arcuate foramen presented as follows: Bilateral: 18 Left: 32 Right: 28	It is indicated that the presence of arcuate foramen should be examined on radiographs before screw placement in the lateral mass of the atlas to avoid injury to the vertebral artery.
Karau et al. 2010	Kenya	Not documented/Female 53 Male 49	29/102	Vertebrobasilar insufficiency and vertebral artery dissection	CD	Arcuate foramen presented as follows: Left: 14 Right: 15	Risk of vertebrobasilar insufficiency, vertebral artery dissection and cervicogenic syndromes
Kavaklı et al. 2004	Turkey	Not documented/Not documented	19/86	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 9 Left: 8 Right: 2	Possible compression of the vertebral artery during neck rotation movements causing symptoms of vertebrobasilar insufficiency

CT, computed tomography; ESP, Elongated Styloid Process; DD, Donor dissection; Rx: x-Ray; PP, ponticulus posticus (arcuate foramen).
*,** indicates a *P*-value less than 0.05 is considered significant.

Continues

Table 2. Continued

Author/year	G. Region	Age Mean/Sex	F.I. (Number of Cases/Total of Cases) Prevalence	Symptoms	Evaluation Mode	Type of Variant	Clinical Implications
Kendrick and Biggs. 1963	USA	Not documented/Female 189 Male 164	56/353	Not documented	Rx	Arcuate foramen presented as follows: Bilateral: 30 Unilateral: 56	Not documented
Khanfour et al., 2015	Egypt	Not documented/Not documented	6/25	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 1 Left: 3 Right: 2	Better preoperative planning to avoid injuries to the third segment of the vertebral artery and thus reduce the risk of complications related to surgical approaches.
Kobayashi. et al. 2008	Japan	62 ± 16/Female 11 Male 35	5/50	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 2 Left: 3	Preoperative evaluation is suggested for orthopedic surgeries that compromises the posterior arch of C1.
Krishnamurthy et al., 2007	India	Not documented/Not documented	87/1044	Not documented	CDD	Arcuate foramen presented as follows: Bilateral: 12 Left: 48 Right: 27	Association with symptoms such as vertigo, dizziness, headaches, shoulder, arm and neck pain due to compression of the vertebral artery.
Kuhta et al. 2010	USA	Not documented/Not documented	112/244	Not documented	Rx	Not documented	Risk of vertebrobasilar insufficiency and vertebral artery dissection.
Lalit. et al., 2014	India	Not documented/Not documented	10/60	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 2 Left: 5 Right: 3	Implication in the possible appearance of vertigo, dizziness, nausea, diplopia and other neurological disorders due to compression of the vertebral artery.
Lamberty and Zidanovic. 1973*	England	Not documented/Not documented	146/1050	Dizziness, vertigo, pain in the arm and occipital area.	CD + Rx	Arcuate foramen presented as follows: Bilateral: 39 Unilateral: 107	Vertebrobasilar insufficiency.
Lee et al. 2006	USA	Not documented/Female 252 Male 457	191/709	Not documented	CD	Not documented	Prevention of injuries to the vertebral artery due to the use of screws in the C1 vertebra during surgical procedures.

Limousin. 1980	Argentina	Not documented/Not documented	30/30	Symptoms associated with Barré-Liéou syndrome (vertigo, dizziness, occipital headaches)	CT	Not documented	Relief of symptoms associated with Barré-Liéou syndrome due to vertebral artery compression.
Malukar et al. 2011	India	Not documented/Not documented	14/80	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 6 Left: 5 Right: 3	Importance for presurgical planning in operations in which screws are used to fix cervical vertebrae, in addition to association with Barré-Liéou syndrome.
Mitchell. 1998	South Africa	Not documented/Not documented	147/264	Not documented	CD	Not documented	Compression of the vertebral artery due to sudden rotation of the neck causing possible vertebrobasilar ischemia.
Mitchell. 1998	South Africa	20. −79/Female 762 Male 1946	264/2708	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 84 Left: 65 Right: 31	Vertebrobasilar insufficiency due to compression of the vertebral artery during lateral rotation movements of the head and neck.
Mudit et al. 2014	India	20.2/Female 360 Male 290	19/650	Not documented	Rx	Not documented	Surgical implication, not knowing this variation could have fatal consequences. Furthermore, the presence of the arcuate foramen is associated with orofacial pathologies, migraines and chronic tension headaches.
Ossenfort., 1926	USA	45/Female 31 Male 152	22/183	Not documented	CD	Not documented	Not documented
Paraskevas., 2005	Greece	Not documented/Female 86 Male 990	18/176	Symptoms of vertebrobasilar insufficiency	CD	Not documented	Vertebral artery compression triggering vertebrobasilar insufficiency.
Patel. et al. 2012	India	Not documented/Not documented	13/100	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 1 Unilateral: 12	Possible vertebrobasilar insufficiency, it is indicated to suspect symptoms such as headaches, vertigo and shoulder or arm pain.
Perez et al. 2014	Peru	14.05 ± 7.43/Female 559 Male 457	209/1016	Not documented	Rx	Not documented	Association with symptoms such as occipital headaches, vertigo and nausea in addition to possible significance in the prognosis of the stabilization of the atlas-axis vertebral complex.

CT, computed tomography; ESP, Elongated Styloid Process; DD, Donor dissection; Rx: x-Ray; PP, ponticulus posticus (arcuate foramen).
*,** indicates a *P*-value less than 0.05 is considered significant.

Continues

Table 2. Continued

Author/year	G. Region	Age Mean/Sex	F.I. (Number of Cases/Total of Cases) Prevalence	Symptoms	Evaluation Mode	Type of Variant	Clinical Implications
Pyo and Lowman. 1959	USA	47.1/Female 170 Male 130	38/300	Not documented	Rx	Not documented	Importance as a radiological finding to take into consideration in lesions of the posterior cranial fossa or the cervical segment of the spinal cord in its most superior portion.
Radojevic y Negovanovic.1963	Yugoslavia	Not documented/Not documented	39/1200	Among people who have the variation, it is reported that the x-ray was performed in 8 cases for epilepsy, 7 for brain tumors and 6 for suboccipital neuralgia.	CD + Rx	Arcuate foramen presented as follows: Bilateral: 14 Left: 15 Right: 13	Relevance at a radiological level to differentiate pathological states with normality.
Romanus and Tovi., 1964	Sweden	40.8/Female 51 Male 54	15/105	Not documented	Rx	Arcuate foramen presented as follows: Bilateral: 6 Unilateral: 9	Not documented
Sabir et al., 2014	India	Not documented/Not documented	119/400	Neck pain, cervicogenic headaches and migraines with and without aura	Rx + CT	Not documented**	Arcuate foramen is easily visible on lateral cephalograms and may be associated with migraines. Radiographic detection of this variation should be considered an important task, as this abnormality may be a key indicator of underlying pathological processes. Additionally, surgical excision appears to relieve symptoms such as headaches, vertigo, and basilar insufficiency.
Saunders and Popovich., 1978	Canada	male 38.8/female 36.5/ Female 296 Male 296	55/592	Not documented	Rx	Not documented	The Atlas bridge appears at an average age of 10.7 years, demonstrating that they are not simply expressions of soft tissue sclerosis in old age. The trait is more common in relatives of affected individuals than in the sample as a whole.

Schilling et al., 2010	Chile	18.44/Female 263 Male 173	40/436	Not documented	Rx	Not documented	It suggests that arcuate foramen is an anatomical condition intended to protect the passage of the vertebral artery and should not be considered a calcification with pathological significance.
Sekerci et al., 2015	Turkey	32.7/Female 295 Male 247	70/542	Patients with different problems in the maxillofacial region	CT	Arcuate foramen presented as follows: Bilateral: 36 Unilateral: 34	There is a significant correlation between the presence of PP and ESP, suggesting that patients with PP are more likely to have ESP. The importance of considering both conditions in clinical evaluations is highlighted, especially when planning surgical interventions, and the need to use three-dimensional imaging techniques, such as CT, is emphasized to avoid complications during procedures in the cervical spine.
Sekerci et al., 2015	Turkey	24.8/Female 385 Male 313	88/698	Not documented	CT	Arcuate foramen presented as follows: Bilateral: 44 Unilateral: 44	The prevalence of PP is higher than expected, being a common anomaly in the Turkish population.
Selby et alt., 1955	USA	Not documented/Female 178 Male 128	37/447	Not documented	Rx	Not documented	This trait is not pathological, it is not rare or excessively common, and it is undoubtedly inherited.
Senoglu et al., 2006	Turkey	44.6/Female 28 Male 144	27/338	Neck and/or arm pain	CD + Rx	Arcuate foramen presented as follows: in x-rays not documented in corpse Two-sided: 8 Left: 8 Right: 2	Know the presence or absence of the variation can be useful for planning surgeries in the C-1 region, allowing the risks of the procedure to be explained for the patient. Furthermore, knowing this variant allows us to reduce the number of lesions in the vertebral artery during a C-1 laminectomy.

CT, computed tomography; ESP, Elongated Styloid Process; DD, Donor dissection; Rx: x-Ray; PP, ponticulus posticus (arcuate foramen).
*,** indicates a *P*-value less than 0.05 is considered significant.

Continues

Table 2. Continued

Author/year	G. Region	Age Mean/Sex	F.I. (Number of Cases/Total of Cases) Prevalence	Symptoms	Evaluation Mode	Type of Variant	Clinical Implications
Sharma et al., 2010	India	15/Female 558 Male 300	37/858	Not documented	Rx	Not documented	The finding of PP can be of great importance for patients during a surgical intervention of the cervical spine, especially in those who require screws in the atlas region. It is not an uncommon anomaly in the Indian population. In addition, it can become important in certain cases of headaches and migraines. Therefore, the cephalogram should be viewed as a basic evaluation tool to detect abnormalities and pathologies in the cervical spine region.
Shinde and Mallikarjun., 2012	India	Not documented/Not documented	2/67	Not documented	CD	Arcuate foramen presented as follows: Left: 1 Right: 1	Although some authors propose the hypothesis that the presence of an abnormal bone hole may have a protective function for the vertebral artery, it can also generate compression and hinder the blood supply to the vertebral artery. Surgeons, neurosurgeons, Anesthetists and radiologists should be aware that this variation can cause headaches, vertigo, vertebrobasilar insufficiency and unexplained shoulder pain.
Simsek et al., 2008	Turkey	Not documented/Not documented	6/158	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 1 Left: 3 Right: 2	This study indicates the importance of recognizing this anomaly of the C1 vertebra. Know the Posterior arch variations may be useful for surgeons dealing with craniocervical junction procedures.

Taitz and Nathan., 1986	Israel	11—105/Not documented	53/672	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 22 Unilateral: 31	If the arcuate foramen is small, normal movement of the vertebral artery may be restricted. The study of the arcuate foramen could facilitate the interpretation of radiological findings, guide neurosurgical situations and perhaps be considered as a precaution when performing craniovertebral manipulation.
Tetradis and Kantor., 1999	USA	14.8/Female 191 Male 134	325/365	Not documented	Rx	Not documented	In routine radiographs of orthodontic patients, 431 incidental radiological findings were found. These findings require cephalometric analysis evaluation. In addition to correctly interpreting positive findings that require treatment or referral. Cephalometric radiographs should be performed interpreted by a specialist familiar with the anatomy, normal variants and anomalies of the oral, maxillofacial and head and neck structures.
Travan et al., 2011	Italy	Not documented/Female 51 Male 71	13/180	Not documented	CD	Not documented	It has been found that the arcuate foramen determines the gross compression of the third segment of the vertebral artery. This situation can predispose to compression of the vertebral artery, mainly during movements of the atlas. Bone and arterial abnormalities can, individually or in combination, cause a reduction in cerebral blood flow.

CT, computed tomography; ESP, Elongated Styloid Process; DD, Donor dissection; Rx: x-Ray; PP, ponticulus posticus (arcuate foramen).
*,** indicates a *P*-value less than 0.05 is considered significant.

Continues

Table 2. Continued

Author/year	G. Region	Age Mean/Sex	F.I. (Number of Cases/Total of Cases) Prevalence	Symptoms	Evaluation Mode	Type of Variant	Clinical Implications
Tubbs et al., 2007	USA	73/Female 21 Male 39	3/60	Not documented	CD	Not documented	The presence of PP may compress the V3 segment of the vertebral artery based on the results of this postmortem study. However, the study does not identify the presence of symptoms. Based on the literature, symptoms caused by compression of the vertebral artery can be relieved by surgical procedures. The neurosurgeon must take this anatomical variation into consideration when performing surgery in the region near C1.
Unur et al., 2004	Turkey	42.6/Female 243 Male 108	18/351		Rx	Arcuate foramen presented as follows: Bilateral: 3 Left: 7 Right: 8	The data obtained reflect one of the morphological characteristics of the Atlas in the Turkish population. The contribution of the presence of PP to the clinical findings of vertebrobasilar insufficiency should be evaluated through additional studies.
Veleanu et al., 1977	Rumania	Not documented/Not documented	39/71	Not documented	CD	Arcuate foramen presented as follows: Bilateral: 19 Left: 5 Right: 15	Not documented
Wysocki et al., 2003	Poland	Not documented/Female 37 Male 63	13/100	Not documented	CD	Not documented	Variants of development of the cervical vertebrae, especially C1 and C2, can produce a series of disorders such as headaches, vertigo, tinnitus, paresis or paralysis of the extremities. These developmental disorders should always be taken into account during planning the diagnostic process in obese patients with disorders within the hearing organ.

Yamaguchi et al., 2008	Japan	55.5/Female 71 Male 69	13/140	Not documented	CT	Arcuate foramen presented as follows: Bilateral: 5 Unilateral: 8	To avoid involuntary VA injuries during surgery at the craniocervical junction, surgeons must be aware of the location and branches of the vertebral artery because they can have significant variations in each patient. Preoperative recognition of the configuration of the vertebral artery and surrounding structures should be considered in cases where the vertebral artery or its branches are considered problematic during surgery.
Young et al., 2005	USA	Not documented/Not documented	76/490	Not documented	DD + Rx	Arcuate foramen presented as follows: Bilateral: 1 Unilateral: 3	It is suggested that PP is a common anomaly that can be easily confused for a wide posterior arch of the atlas. It is recommended that before placing a screw in what appears to be a widened posterior arch of the atlas, the surgeon should review the neck x-ray for the presence of PP.

CT, computed tomography; ESP, Elongated Styloid Process; DD, Donor dissection; Rx: x-Ray; PP, ponticulus posticus (arcuate foramen).
*,** indicates a *P*-value less than 0.05 is considered significant.

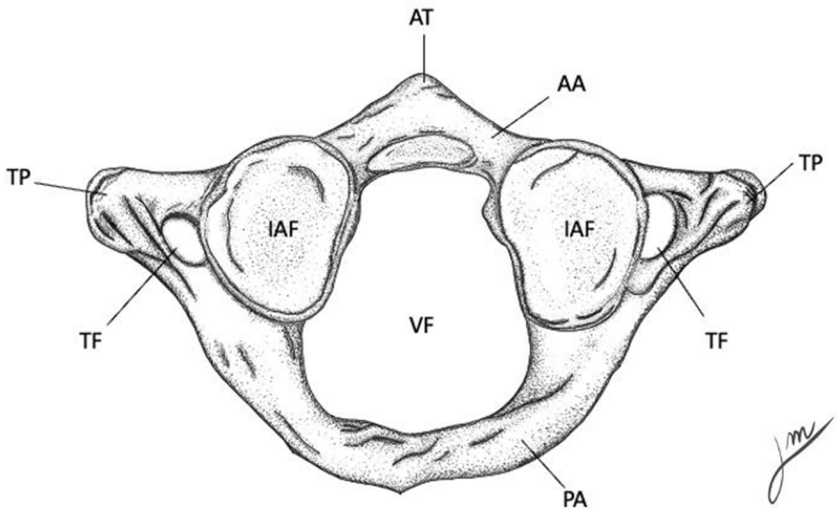

Figure 2. Inferior view of atlas vertebrae. AT, anterior tubercle; AA, anterior arch; PA, posterior arch; IAF, inferior articular facet; TF, transverse foramen; TP, Transverse foramen; VF, vertebral foramen.

potentially relevant. If the two reviewers could not reach a consensus, a third reviewer (Rojas C) was involved in the decision-making process. Additionally, we performed an agreement test between the authors using the kappa statistic to evaluate reliability and the risk of bias among the reviewers. The calculated kappa value was 0.61, indicating good agreement.

Data Collection Process

Two authors (Nova P and Sanchis J) independently extracted data on the outcomes of each study. The following information was collected from the included studies: *1) authors and year of publication*, *2) geographical region*, *3) age and sex of participants*, *4) sample size and prevalence*, *5) symptoms*, *6) contextual circumstances*, *7) characteristics of variants*, *and 8) clinical considerations*.

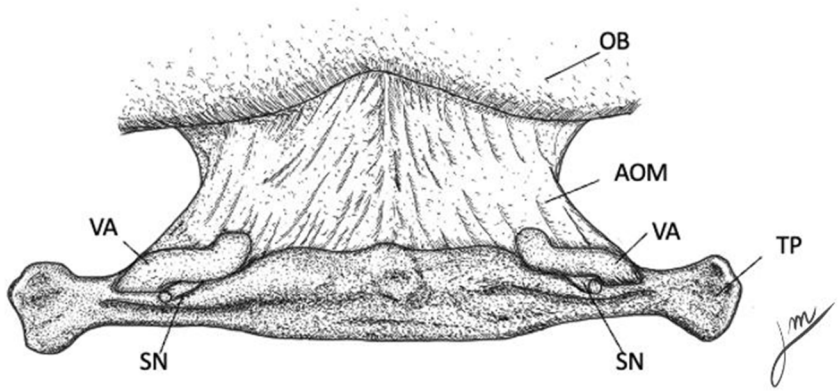

Figure 3. Posterior view of atlas vertebrae. OB: occipital bone; AOM: atlantooccipital membrane; VA: vertebral artery; SN: Suboccipital nerve; TP: transverse process of atlas.

Assessment of the Methodological Quality of the Included Studies

To assess the bias of the included studies, we utilized the verification for anatomical studies (AQUA) proposed by the International Working Group on Evidence-Based Anatomy (IEBA).[16] Two authors (Valenzuela JJ and Nova P) independently analyzed the 5 domains outlined by the AQUA tool. After their evaluations, they reached a consensus and created the bias graph.

Statistical Methods

The data extracted from the meta-analysis was analyzed using R statistical software (accessed in October 2024) to calculate the prevalence of CC morphological variants. The DerSimonian-Laird model and a Freeman-Tukey double arcsine transformation combined the summary data. A random effects model was used due to the high heterogeneity observed in the prevalence data of AF.[6] To assess the degree of heterogeneity among the included studies, we utilized the chi² test and the I^2 statistic. For the chi² test, a P value of 0.10 was considered significant, as suggested by the Cochrane collaboration. The values of the I^2 statistic were interpreted with a 95% confidence interval (CI) as follows: 0%–40% indicates no significant heterogeneity, 30%–60% suggests moderate heterogeneity, 50%–90% reflects substantial heterogeneity, and 75%–100% denotes a considerable amount of heterogeneity.[11] To evaluate the presence of a small-study effect (the phenomenon that smaller studies may show different effects than large ones), a Doi plot with the LFK index was generated.[17,18]

Subgroup Analysis

To avoid bias in estimating the differences in results between the subgroups of FA morphological variants, we conducted the same statistical analysis for these subgroups. Additionally, we included each subgroup's prevalence and conducted qualitative assessments regarding clinical considerations. The subgroups were classified as imaging samples, and donor samples. We also

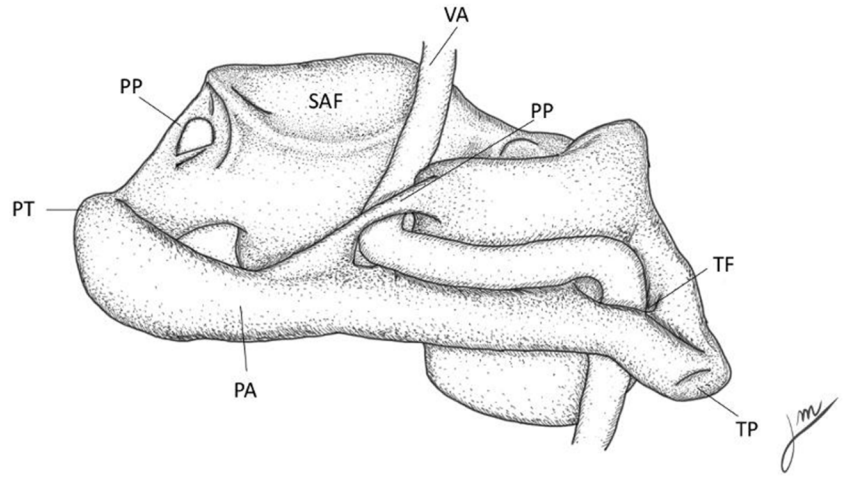

Figure 4. Lateral view of atlas vertebrae. PT, posterior tubercle; PA, posterior arch; PP, Ponticulus Posticus; SAF, superior articular facet; VA, vertebral artery; TF, transverse foramen; TP, Transverse process.

classified them based on geographical regions, FA morphological variants, and subgroups categorized by male and female participants, with each group analyzed individually.

RESULTS

Characteristics of Included Studies

The total number of included studies was 65 and the total number of individuals analyzed was 27.731, with a prevalence of AF found in 3.649 individuals.[8,9,11,19-80] Regarding geographical location, 19 articles were conducted in America, 9 in Europe, 31 in Asia, 6 in Africa, and 1 in Oceania. Regarding the gender of the individuals included in the study, 9.947 were men, 9.763 were women, and 8.021 were not reported. In relation to the average age, among the articles that mentioned AF, an average of 37.1 years was found (**Figure 1** and **Table 2**).

Detailed Anatomical Description

AF is an anatomical anomaly present in the first cervical vertebra or atlas, where bony growth occurs over the third segment of the VA (V3). This growth is located posterior to the lateral mass of the posterior arch of the atlas and forms due to the calcification of the oblique atlanto-occipital membrane at the junction between the spine and the skull.[33] The formation of this bony bridge creates a foramen that contains the VA, the suboccipital nerve, and the cervical venous plexus.[11] Moreover, the atlanto-occipital membrane is connected to the dura mater, so small tensions exerted on the dura mater may lead to ischemia in the posterior circulation, potentially causing cervicogenic headaches.[56,81-84]

In the literature, various authors describe different AF classification systems, leading to a lack of current consensus regarding the classification of this anatomical variant.[54] One of the most commonly used classifications is that of Wight et al. (1999),[85] which categorizes AF as absent, incomplete, or complete.[79] Other authors, such as Hasan et al. (2001), classify AF into 6 types based on the characteristics of the posterior arch related to the passage of the VA (**Figures 2–4**).[9] Cederberg et al. (2008)[27] described 4 degrees of ossification: Grade 1, no calcification; Grade 2, calcification of less than 50% of the VA groove; Grade 3, calcification greater than 50% of the groove; and Grade 4, complete calcification of the groove.[21] Finally, another classification used is that of Nedelcu et al. (2016)[86] who describe 5 types of AF classification; Type I unilateral incomplete; Type II, bilateral incomplete; Type III, unilateral complete; Type IV (mixed), a unilateral complete bridge with a contralateral incomplete bridge; and Type V, bilateral complete.[86]

Prevalence of the Arcuate Foramen and Distribution (or Location). Regarding anatomical variation, a type IV or complete variation was defined as an AF. Among the 27.731 individuals analyzed across all studies, 3.481 were classified as exhibiting an AF. Of these, 17 articles categorized anatomical variations by gender, reporting 363 men and 513 women.

Furthermore, bilateral and unilateral (right or left) localization were also assessed. Of the 65 reviewed studies, 27 did not specify the presentation of an AF. In those studies that did specify, AF was identified as bilateral in 609 cases, left-sided in 347 cases, and right-sided in 264 cases. Notably, 10 studies only indicated whether the AF was bilateral or unilateral, without specifying laterality. In these instances, an AF was reported as unilateral in 283 cases, with no further laterality specification.

Concerning the study methodology, 19 of the 65 reviewed articles employed donor material observation. In all, 32 studies utilized both donor observation and imaging techniques, while 28 studies relied on radiological analysis.

Fourteen-proportion Forest plots were created to calculate the prevalence of AF morphological variants in the studies included in this systematic review. For the overall prevalence, 65 studies were included that presented an overall incidence of 16% of AF variants (CI: 11% to 20%) (**Figure 5**).[8,9,11,19-80] This prevalence exhibited an LFK index of 0.147, indicating asymmetry and publication bias in this prevalence analysis (**Figure 6**). For the individual analysis, the variables were grouped into different subgroups. In the first subgroup, the prevalence was calculated according to the type of sample of subjects who presented an AF in the atlas. This subgroup analysis included donor samples, imaging-based samples, and studies that incorporated both methods. A total of 28 studies were included in the donor sample group.[9,19,20,26,30,35-37,39,40,42-44,46,48,50-52,54-56,70-72,74,75,77,78] For this sample, the prevalence was 14%, with a CI ranging from 9% to 19% and a

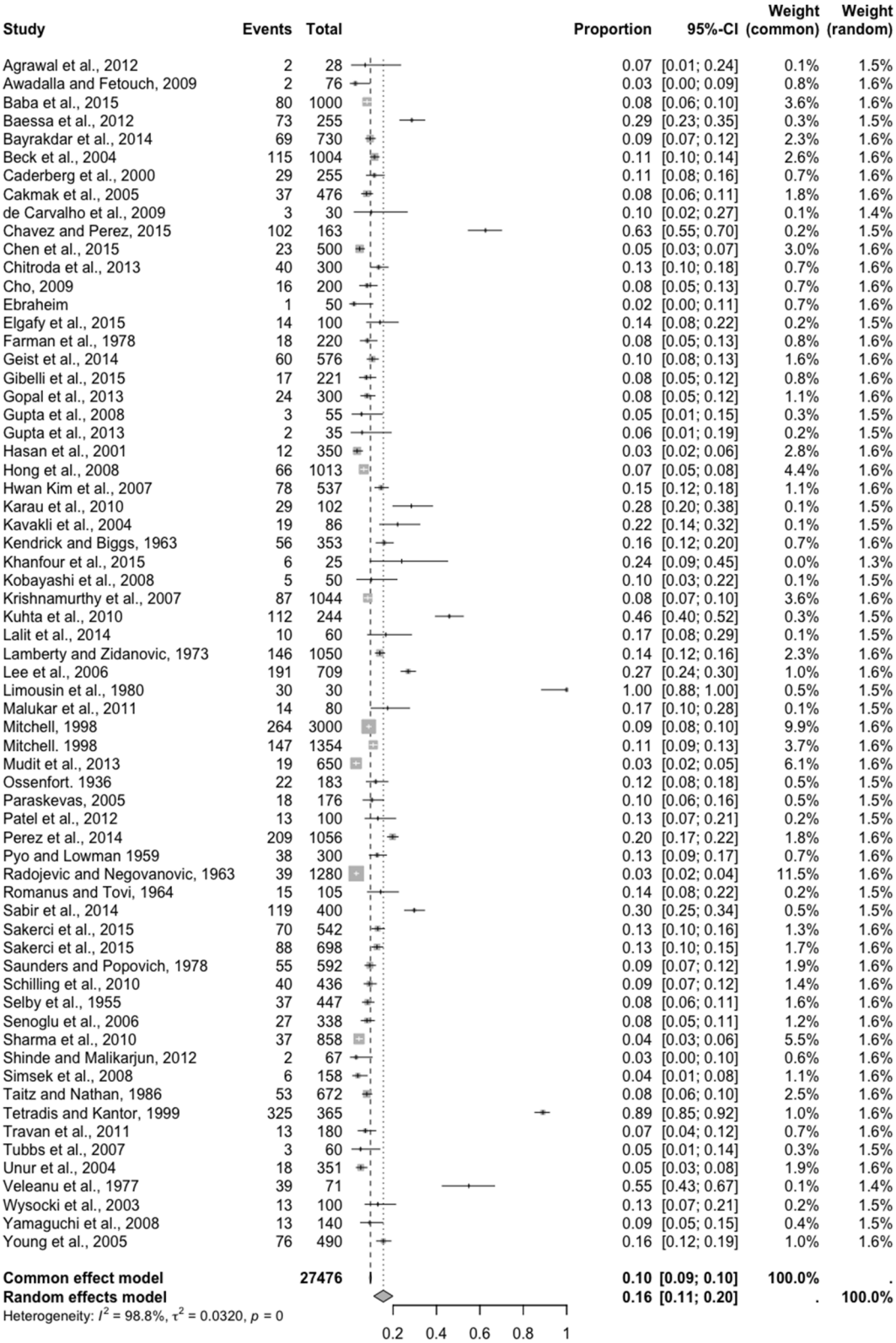

Figure 5. All included articles Forest plot.

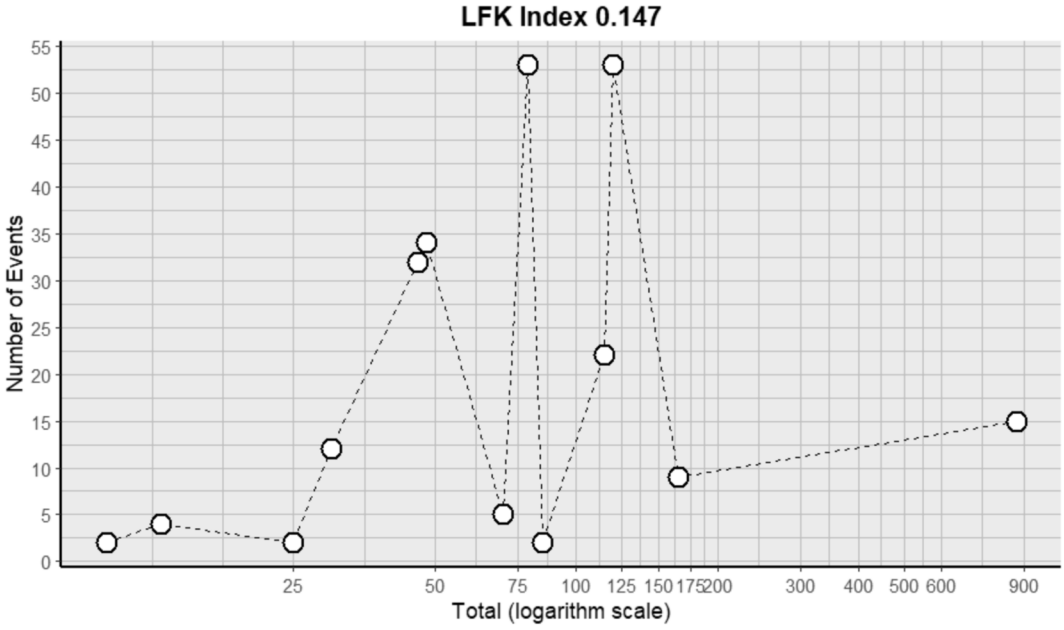

Figure 6. Doi plot prevalence total studies included.

sample heterogeneity of 95% (Figure 7). This prevalence exhibited an LFK index of 0.15, indicating asymmetry and publication bias in this prevalence analysis (Figure 8).

For the imaging sample, 32 studies were included.[8,11,21-24,27-29,31-34,37,41,45,49,53,57-59,61-67,69,73,76,79] For this pooled sample, the prevalence was 17%, with a CI ranging from 10% to 25%, and a sample heterogeneity of 99.3% (Figure 9). This prevalence exhibited a Doi plot with an LFK index of 0.134, indicating asymmetry and publication bias for this prevalence analysis (Figure 10). For the donor and imaging sample, studies were included.[25,47,60,68,80] For this sample, the prevalence was 10%, with a CI ranging from 5% to 14%, and a sample heterogeneity of 97% (Figure 11). This prevalence exhibited an LFK index of 0.04, indicating asymmetry and publication bias for this prevalence analysis (Figure 12). For this subgroup, the mean difference was 0.03, indicating a statistically significant difference in favor of a higher presence of studies where data originated primarily from imaging.

In the second subgroup, the analysis was conducted based on geographical region, considering samples from Asia, Africa, Europe, America, and Oceania. The Asian sample included 31 studies for this sample, the prevalence was 10%, with a CI ranging from 7% to 12%, and a sample heterogeneity of 91% (Figure 13).[7,8,11,19,21-23,25,28,29,35-38,40,43,44,46,50,53,56,62,65,66,68-71,76,79] This prevalence exhibited an LFK index of 0.143, indicating significant asymmetry and publication bias for this prevalence analysis (Figure 14). The American sample included 19 studies for this sample, the prevalence was 22%, with a CI ranging from 10% to 35%, and a sample heterogeneity of 99% (Figure 15).[26,27,30,31,33,41,45,48,49,54,57-59,63,64,67,73,75,80] This prevalence exhibited an LFK index of 0.207, indicating significant asymmetry and publication bias for this analysis (Figure 16).

In the European sample, 8 studies were included for this sample, the prevalence was 15% with a CI of 5% to 25% and a sample heterogeneity of 96% (Figure 17).[34,47,55,60,61,74,77,78] This prevalence showed an LFK index of 0.21, indicating high asymmetry and publication bias in this analysis (Figure 18).

The African sample included six studies for this sample, the prevalence was 21% with a CI ranging from 5% to 37% and a sample heterogeneity of 98.1% (Figure 19).[20,32,39,42,51,52] This prevalence exhibited an LFK index of 0.207, indicating significant asymmetry and publication bias for this analysis (Figure 20). For this geographic region subgroup, the mean difference was 0.123, which indicates no statistically significant difference in the occurrence of the foramen between continents.

In the third subgroup, the analysis was conducted based on sex. The male sample included 18 studies for this sample, the prevalence was 11%, with a CI ranging from 8% to 14%, and a sample heterogeneity of 91% (Figure 21).[7,21,25,31,32,41,53,54,58,61,63-67,69,75,76] This prevalence exhibited an LFK index of 0.327, indicating significant asymmetry and publication bias for this analysis (Figure 22).

The female sample included 18 studies for this sample, the prevalence was 22%, with a CI ranging from 10% to 35%, and a

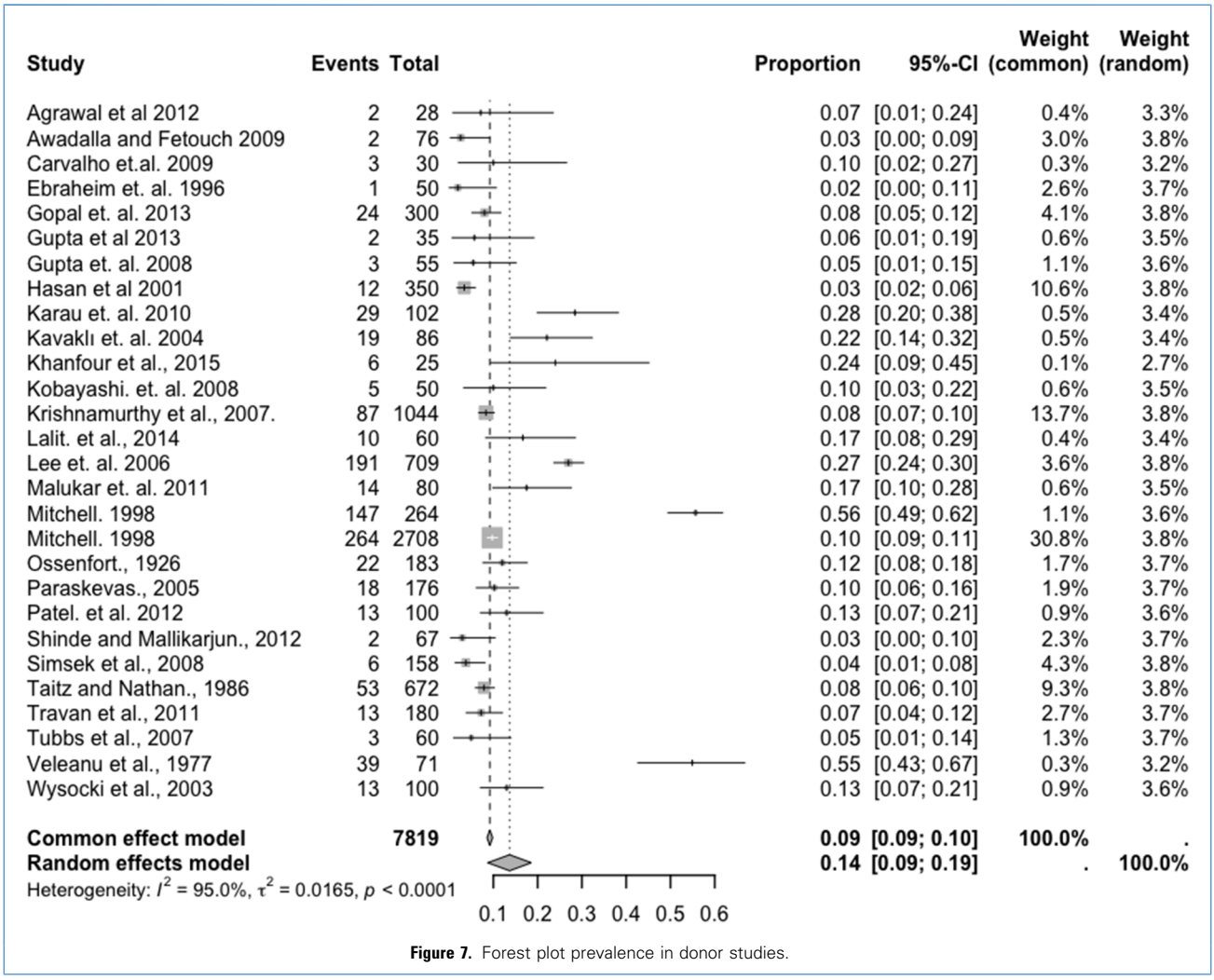

Figure 7. Forest plot prevalence in donor studies.

sample heterogeneity of 99% (Figure 23).[7,21,27,31,32,41,53,54,58,61,63-65,69,75,76] This prevalence exhibited an LFK index of 0.39, indicating significant asymmetry and publication bias for this analysis (Figure 24). For this subgroup, the mean difference was 0.71, indicating no statistically significant differences in the occurrence of an AF between sexes.

In the fourth subgroup, the analysis was conducted based on the laterality of AF occurrence, considering samples from right and left sides. The right-sided sample included 22 studies for this sample, the prevalence was 3%, with a CI ranging from 2% to 4%, and a sample heterogeneity of 80.3% (Figure 25).[8,11,22,25,26,28,31,35,39,40,42,44,46,50,51,60,64,68,70,71,74,76] This prevalence exhibited an LFK index of 0.39, indicating high publication bias (Figure 26). The left-sided sample included 23 studies for this sample, the prevalence was 3%, with a CI ranging from 2% to 4%, and a sample heterogeneity of 77% (Figure 27).[7,9,19,23,25,26,28,31,35,39,40,42,44,46,50,51,60,64,68,70,71,76,78] This prevalence exhibited an LKF index of 0.48, indicating high publication bias (Figure 28). For this subgroup, the mean difference was 0.03, indicating a statistically significant difference in favor of a higher presence of an AF on the left side.

In the fifth subgroup, the occurrence of an AF was analyzed in unilateral versus bilateral forms using the respective samples. The unilateral sample included 10 studies for this sample, the prevalence was 6%, with a CI ranging from 4% to 8%, and a sample heterogeneity of 94% (Figure 29).[29,41,47,56,61,65,66,72,79,80] This prevalence exhibited an LFK index of 0.38, indicating high publication bias (Figure 30).

The bilateral sample included 32 studies for this sample, the prevalence was 4%, with a CI ranging from 3% to 5%, and a sample heterogeneity of 91% (Figure 31).[7,9,19,22,25,26,28,29,31,35,40-44,46,48,50,51,56,60,61,64-66,68,71,72,75,76,79,80] This prevalence exhibited an LFK index of 0.38, indicating high publication bias (Figure 32).For this subgroup, the mean difference was 0.02, indicating a statistically significant difference in favor

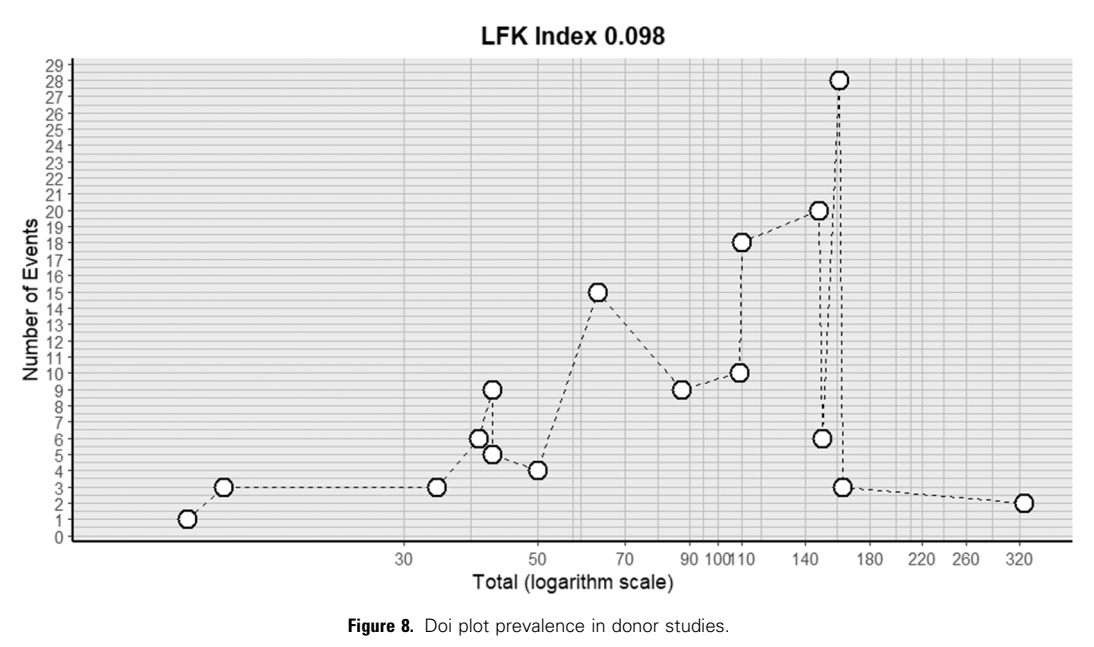

Figure 8. Doi plot prevalence in donor studies.

of a higher presence of an AF in the unilateral form.

Risk of Bias of Included Articles. Thirty-seven studies met the criteria for evaluation using the AQUA Checklist for anatomical studies tool, which analyzed bias in 5 domains. Of the 5 domains offered by the AQUA table, 5 included studies[19,68,71,79,80] presented a high risk of bias in the methodology and characterization domain, while 4 studies[23,41,55,59] had a high risk of bias in the descriptive anatomy domain. Finally, for the reporting of results domain, 8 studies were found to have a high risk of bias, so in at least 10 articles the results should be interpreted with caution (**Figure 33**).[9,22,42,46,47,50,65,68]

Clinical Implications. In 29 studies the importance of surgical planning for procedures such as C1-C2 fusion is highlighted.[7,9,19-23,26,28,29,31,34-38,42,43,48,50,58,65,68,69,71,72,75,79,80] In this surgery, screws are used to fuse the first 2 cervical vertebrae to treat congenital abnormalities, fractures, or degenerative diseases affecting these vertebrae. Failure to consider the presence of an AF can lead to catastrophic consequences, including VA dissection, which may result in hemorrhagic events or even death due to thrombosis, embolisms, or arterial dissection, disrupting blood flow to structures in the posterior fossa like the brain stem and the cerebellum, causing focal symptoms of that area like central vertigo, cerebellar ataxia, affectation of ocular motility or even compromise of the respiratory centers leading to hypoventilation and respiratory insufficiency.

Similarly, 3 studies emphasize the importance of radiological assessment of an AF.[60,72,73] The more this anatomical variation is understood, the more valuable information can be obtained for effective surgical planning, alongside the establishment of clear diagnostic morphological criteria for identifying an AF.

On the other hand, vertebrobasilar insufficiency is characterized by a temporary or permanent decrease in blood flow to the brain. It can have multiple etiologies. In 13 of the analyzed articles, it is suggested that this decreased blood flow may be due to compression of the VA as it passes through an AF.[8,23,33,39,40,45,47,52,55,56,62,70,76] This is especially true during neck flexion, extension, and external rotation movements.[35] As a result of reduced blood flow, symptoms such as vertigo, dizziness, visual disturbances, facial vasomotor alterations, nausea, diplopia, tinnitus, or limb paralysis may occur due to hypoperfusion of the posterior fossa, and compression of the suboccipital nerve or sympathetic plexus.[7,8,24,28,35,39,44-46,52,53,60,62-64,67,68,70,73,74,78]

Additionally, the presence of an AF by itself has been associated with an increased risk of VA dissection, highlighting the importance for chiropractors to consider this variation and to minimize the force applied in cervical manipulations to reduce the risk of this severe complication.[39,45]

Another significant clinical consideration is the association between the presence of an AF and headaches or migraines, as noted in 14 studies.[7,23-25,27,33,44,53,56,58,62,69,70,78] This may occur due to a local meningeal inflammation which could activate the primary nociceptive afferent neurons of the trigeminal nerve. For this reason,

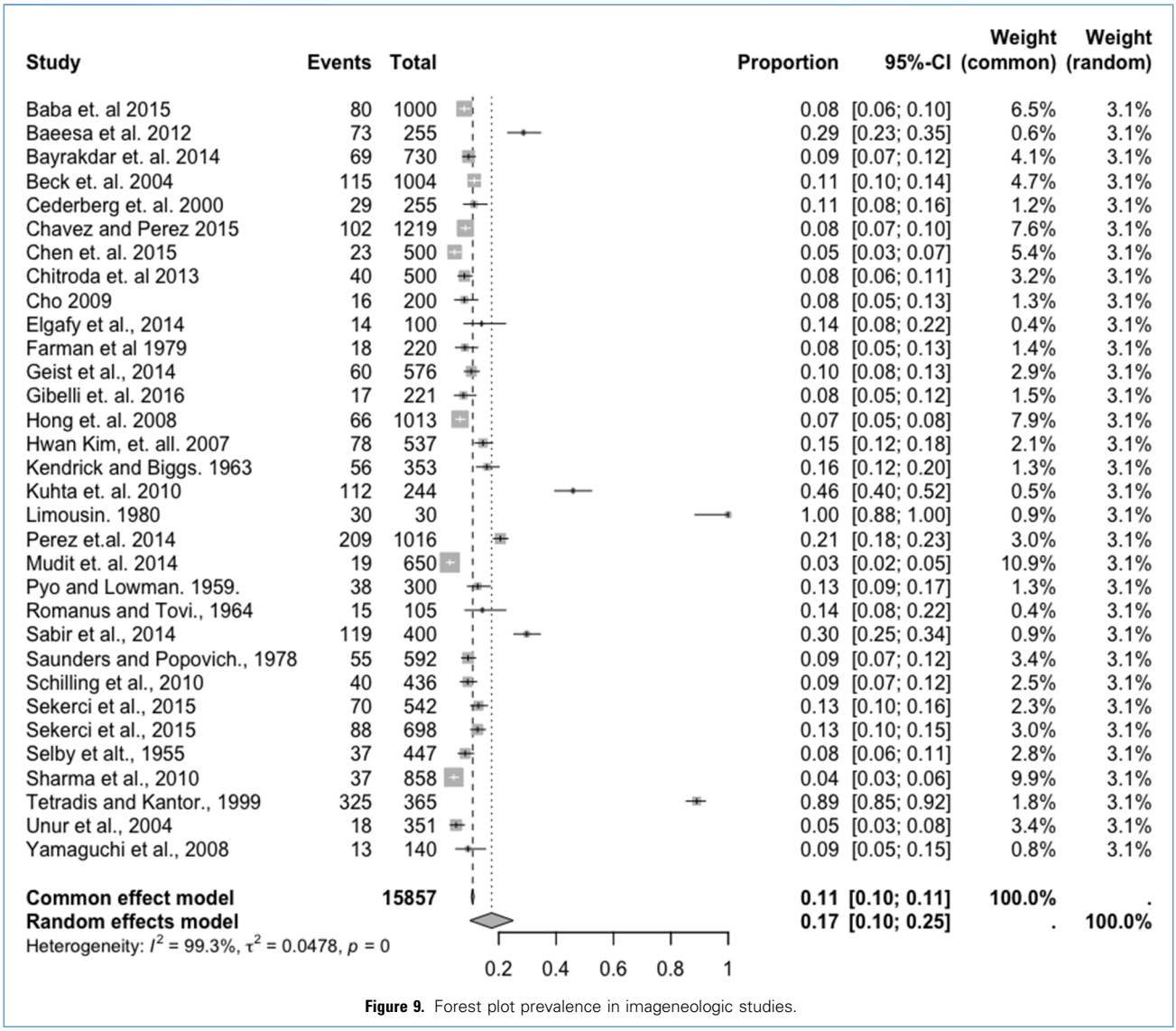

Figure 9. Forest plot prevalence in imageneologic studies.

multiple articles have studied if the presence of an AF can lead to this kind of symptoms given the irritation of the VA in the presence of this anatomical variation. The correct identification of an AF could be useful to reduce misdiagnosis and inadequate treatment of migraines.[81] Additionally, 10 authors report vertigo as a common symptom, making AF a differential diagnosis to consider when dealing with a vertiginous syndrome.[24,25,33,44,46,56,58,62,70,78] Finally, several of the aforementioned symptoms may collectively present as part of Barré-Lieou syndrome, which includes symptoms such as headaches and retro-orbital pain [7,23,24,33,49,50] added to some other authors that describes the presence of shoulder, arm, and neck pain associated with an AF, making it a significant clinical consideration when addressing cervicofacial pain.[25,44,56,71]

DISCUSSION

This meta-analysis is novel due the large amount of data it includes and its emphasis on the diversity of observed clinical findings. It is an excellent tool to visualize the prevalence of this anatomic variation and its relevance in the clinical and surgical fields by considering numerous analytical subgroups that break down AF in the population in a more detailed way. The AF is an anatomic variation that occurs from the ossification of the atlanto-occipital oblique ligament, and it can present in a unilateral or bilateral way. It is relevant because of the prevalence in the population. It is a bony bridge in the posterior arch of the atlas that circumscribes the VA, the suboccipital nerve and the cervical venous plexus. As a result, its presence can cause complications, such as compressing nervous and vascular structures that are proximal to C1 when rotation or lateral flexion movements of the neck are performed, because of that, the study of the AF is essential for the clinical

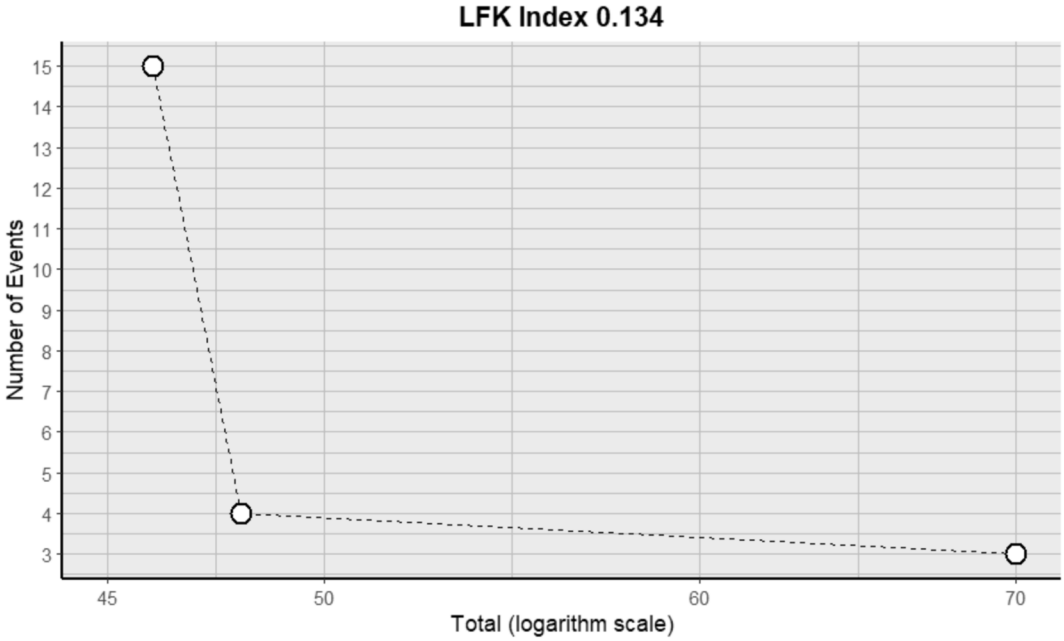

Figure 10. Doi plot prevalence on imageneologic studies.

management in patients who require surgical interventions in the cervical region or that presents cases of vertebrobasilar insufficiency or other syndromes that have been associated with the anatomic variation.

The previous meta-analyses done in this field were mainly centered on the importance of knowing the variant during surgical procedures in the cervical area, and its associated neurological symptoms. Elliot & Tanweer (2014) conducted radiological imaging and donor studies that described the incidence of an AF and utilized meta-analysis techniques to estimate its prevalence in the population.[19] They also discussed the relevance in the surgical insertion of screws in the lateral mass of C1 (C1MLS) through the posterior arch of patients who presented with an AF.[19] The authors included 44 studies on their revision, in which 31 of those articles were included in the present revision. The authors found that

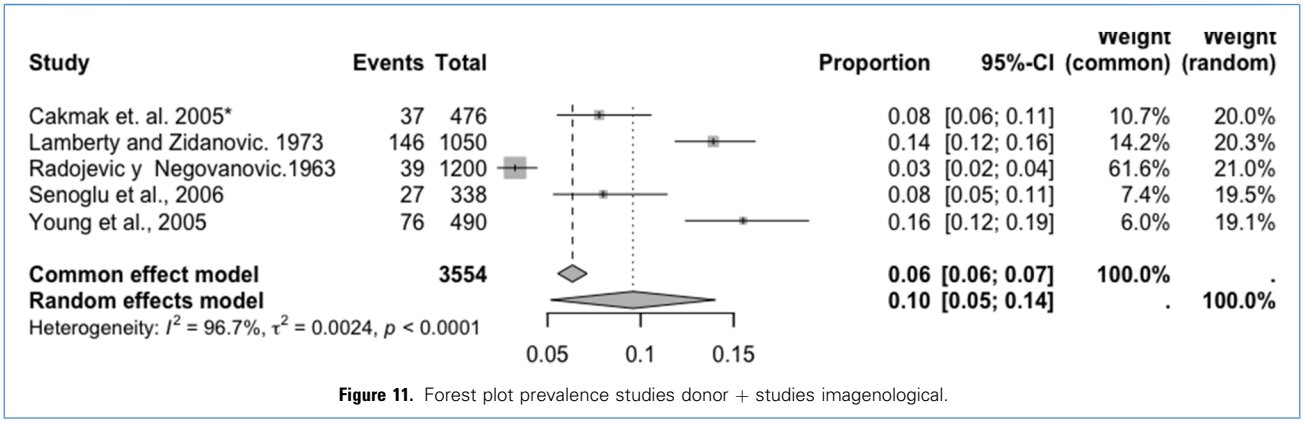

Figure 11. Forest plot prevalence studies donor + studies imagenological.

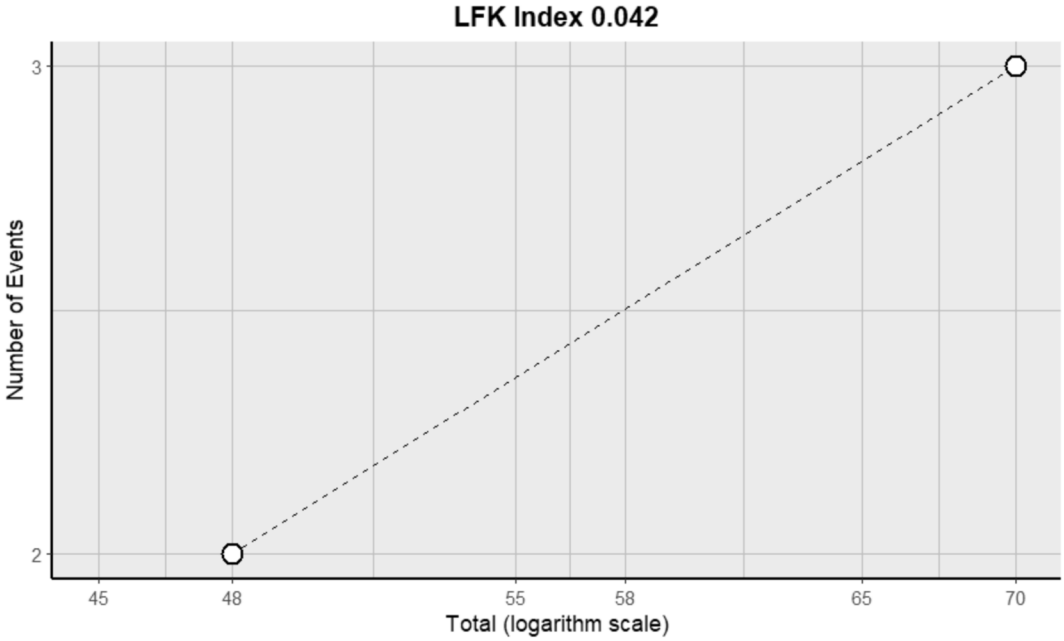

Figure 12. DOI plot prevalence studies donor + imaging studies.

the general prevalence of an AF in the analyzed data is 17%, putting emphasis on the importance of knowing about this anatomic variant due to the increase of patients treated with C1LMS through the posterior arch of the atlas that could expose the patient to lesions in the VA during the procedure. They also mention that in some of the centers where the data was obtained, the prevalence of this anomaly in patients with migraines or cervical discomfort was quite noteworthy. In conclusion, the study indicates that the presence of this anomaly could give a false impression that the posterior arch of the atlas of the patient may have adequate characteristics for the surgical approach of C1LMS, exposing the patient to iatrogenic injury of the VA. For that reason, it's important to know the existence of an AF while performing a thorough evaluation with a preoperatory multiplanar CT that could allow the surgeon to adjust the operation plan following the individual anatomy of the patient, avoiding complications. Pekala (2017) performed a meta-analysis of all the studies with all the extractable data published on the AF.[82] The objective was to generate a more complete investigation of the prevalence of this anatomic variation, while also reviewing the clinical importance of the AF in the neurology and neurosurgery fields. The authors analyzed 116 articles, in which 61 were included in the present revision. The study stands out as being the first to report the prevalence of an AF differentiating between complete and incomplete, where it was found that the presence of complete AF generates neurological symptoms of greater proportion. The study emphasizes the importance of knowing the anomaly given that in the insertion of lateral screws on the atlas, the neurosurgeon may not differentiate between the presence of an AF or a widened posterior arch, which could lead to injury of the VA, a stroke in the vertebrobasilar territory, or even death. Similar to the previous study, the authors emphasize the importance of knowing the presence of an AF due to the increase of this surgical procedure in recent times.

Concluding with the surgical implication of the AF, in this meta-analysis we put great relevance on the consideration of this anatomical variation since an oversight of it could cause the surgeon to inadvertently damage the VA during procedures in the atlanto-occipital area. As a result, it is crucial that both the radiologist and the surgeon are aware of this anomaly and actively look for it through preoperative imaging studies to prevent hemorrhagic events or even patient mortality. Regarding imaging studies, this variant has been documented using lateral cervical radiographs and cone-beam computed tomography (CBCT), with the latter being recognized as more accurate for the evaluation of an AF.[81]

Furthermore, other data supports the direct relevance of the AF in clinical

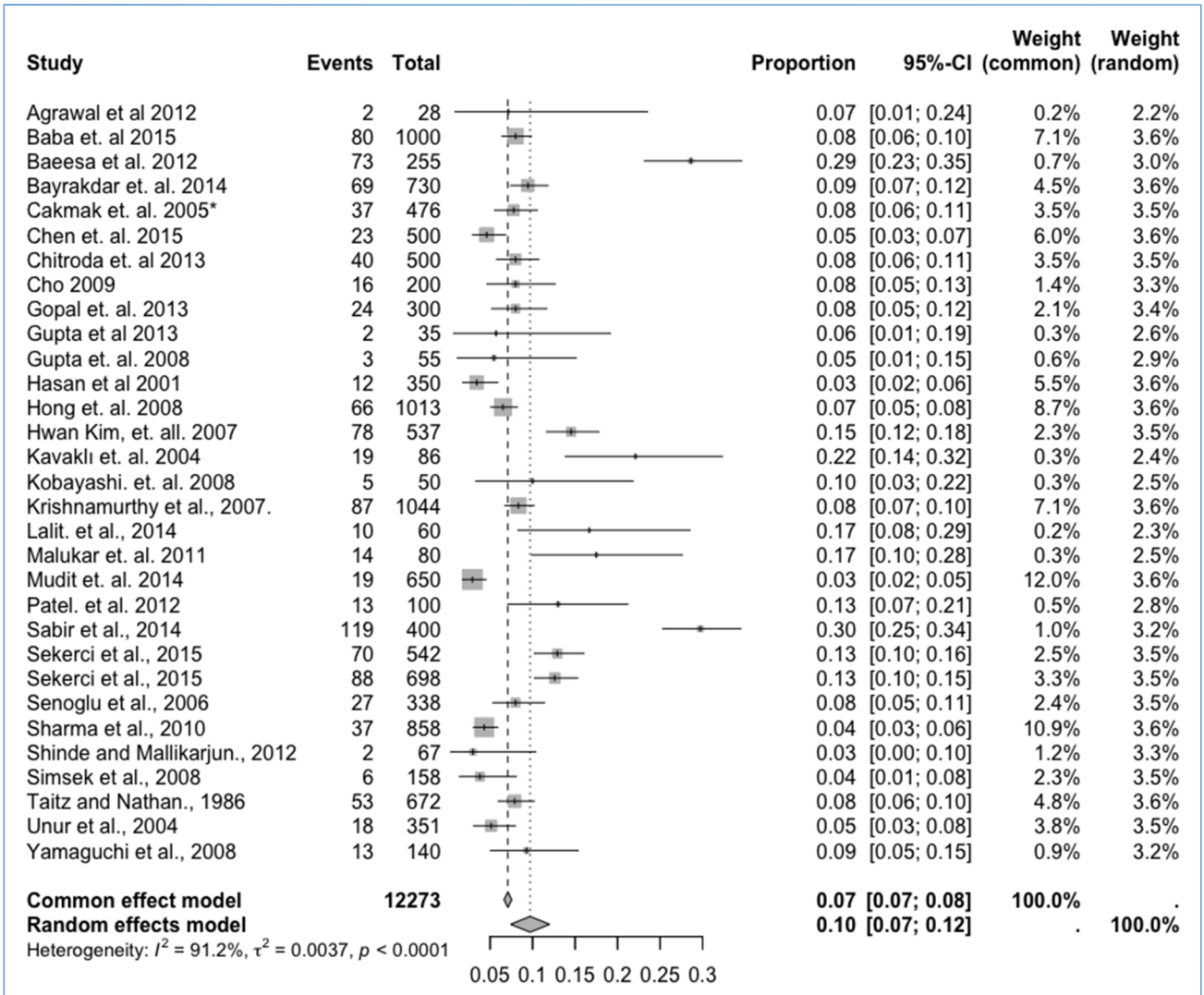

Figure 13. Forest plot prevalence studies from Asia.

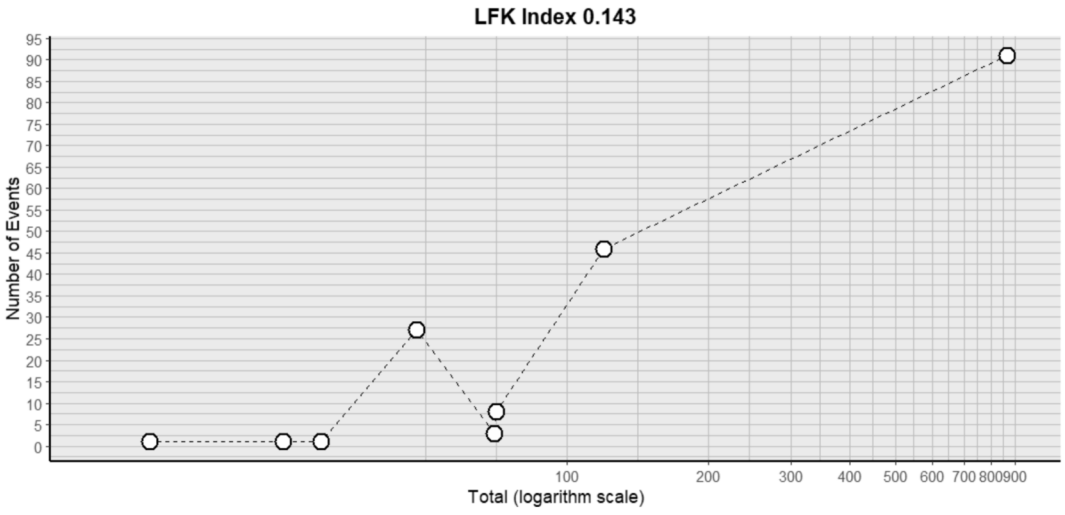

Figure 14. Doi plot prevalence studies from Asia.

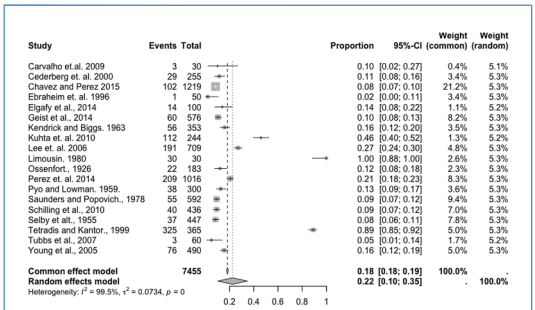

Figure 15. Forest plot prevalence studies from America.

implications. Studies like Pekala (2017) indicate that the neurological symptoms, such as vertigo, migraines and Barré-Liéou syndrome, improve when the AF is surgically removed.[82] The importance of detecting an AF in patients with neurological symptoms associated with the compression of the VA without other explanatory causes is of great importance.

In the same line of thinking, Pekala (2018) performed a meta-analysis on the association of the AF in patients with headaches and migraines with the objective of providing more information about the clinical relevance of this anatomic variation.[83] By collecting data from 10 different articles, the authors not only confirmed that headache is the most prevalent symptom related to the presence of AF, but also showed statistically significant association with migraines without prior aura. Moreover, patients with complete AF presented with headaches in higher proportion than with an incomplete one, meanwhile there was no statistically significant association between unilateral or bilateral AF and the presence of headaches. The authors highlight the importance of the detection of an AF during the characterization of the headaches when the etiology is unknown, given that the symptoms could be related to a vascular origin by the compression of the VA, which occasionally could lead to episodes of ischemia in the vertebrobasilar territory.

It is also important to note the high incidence of migraines with or without aura in patients who present with an AF. Neurologists must be aware of an AF, given that patients may not respond to usual medical treatment the same way that patients without the anomaly do, emphasizing the importance of radiological imaging studies. The exact etiology of migraines is still unknown; however, they are triggered by neurological stimulation that induces the release of inflammatory substances that act temporarily on nerves and brain vessels, generating pain.[81] One study found a statistically significant association between migraines with and without aura and the presence of an AF where VA compression is thought to be

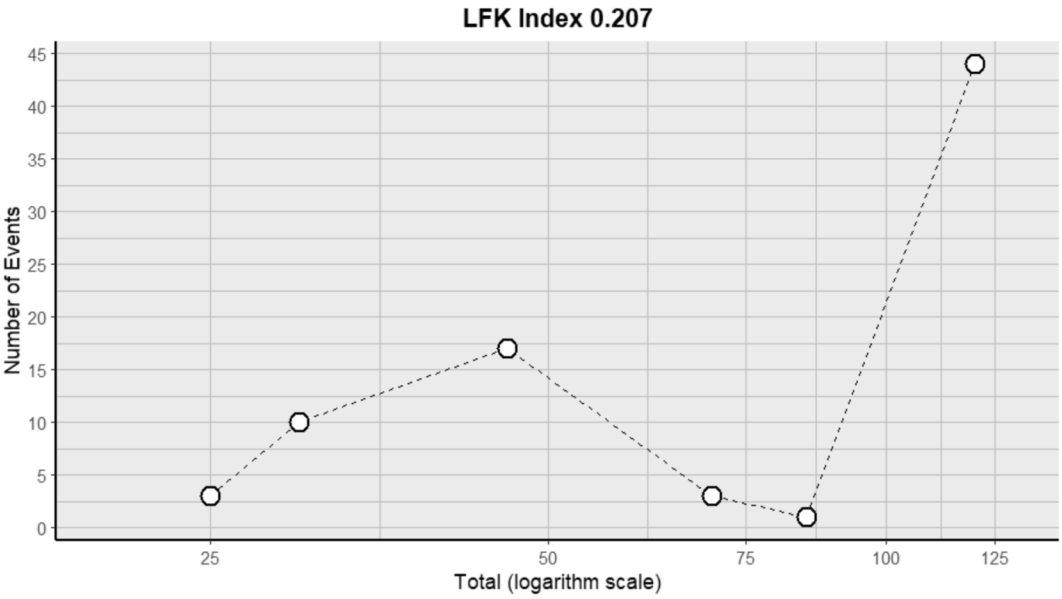

Figure 16. DOI plot prevalence studies from America.

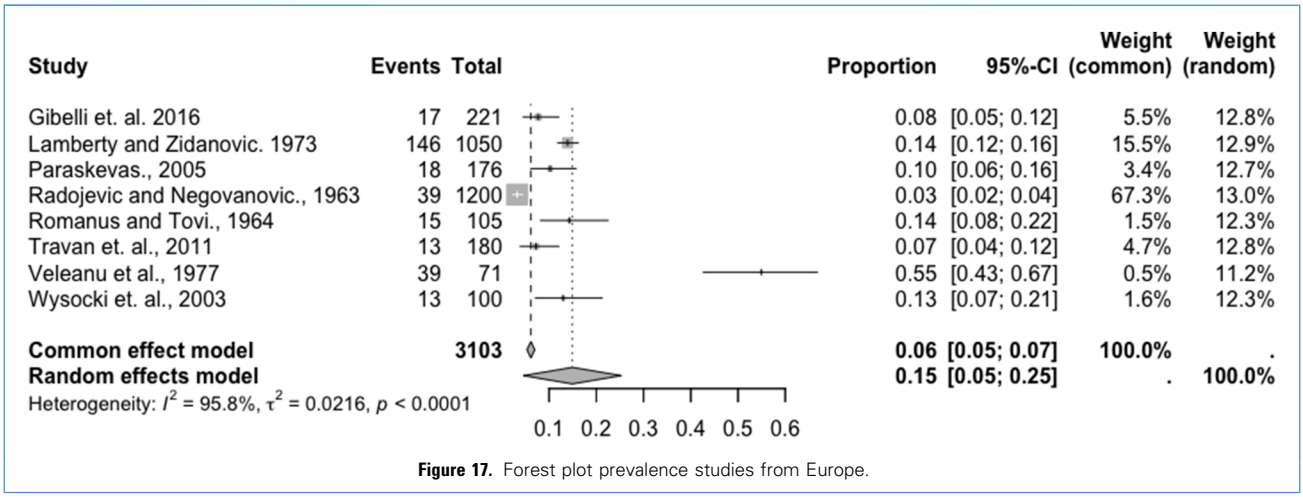

Figure 17. Forest plot prevalence studies from Europe.

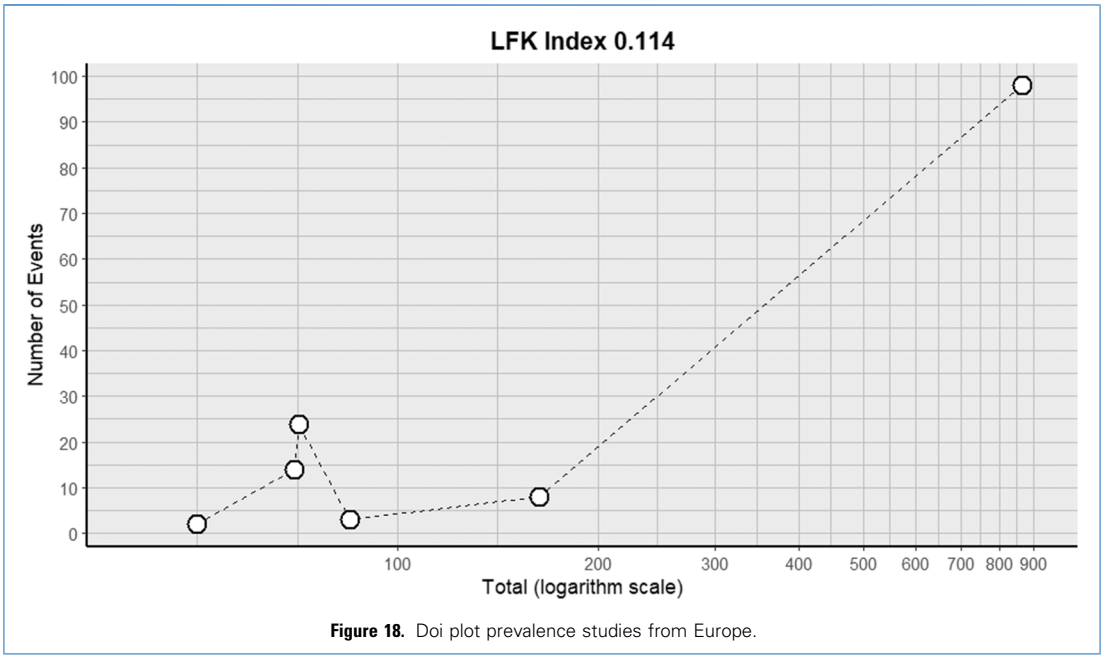

Figure 18. Doi plot prevalence studies from Europe.

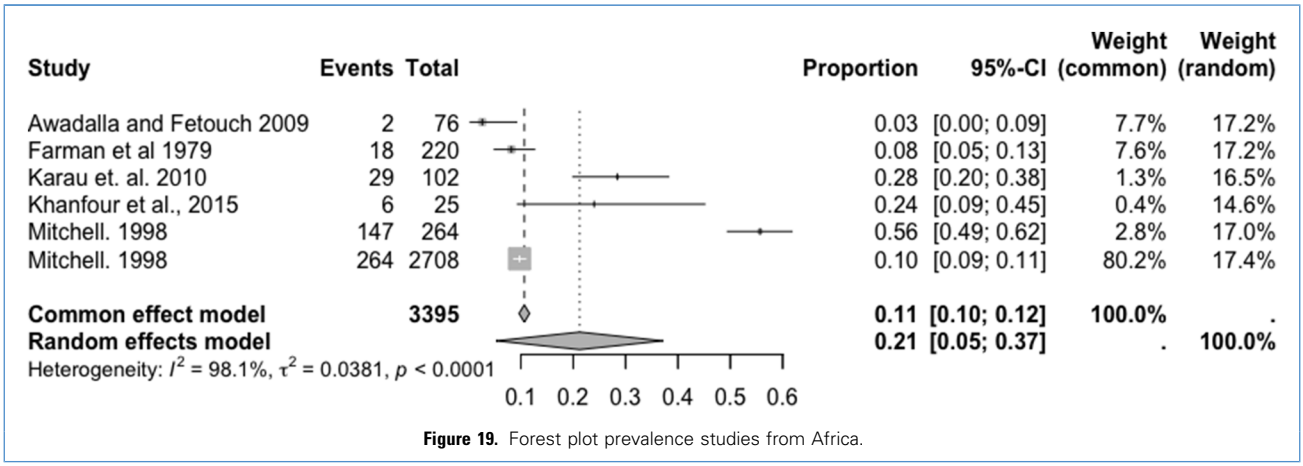

Figure 19. Forest plot prevalence studies from Africa.

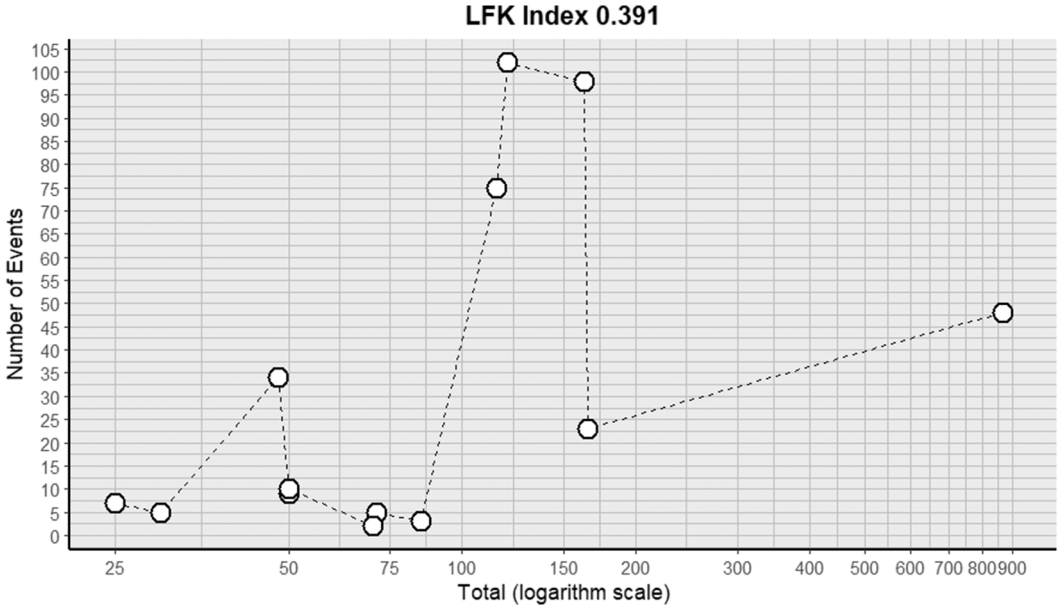

Figure 20. Doi plot prevalence studies from Africa.

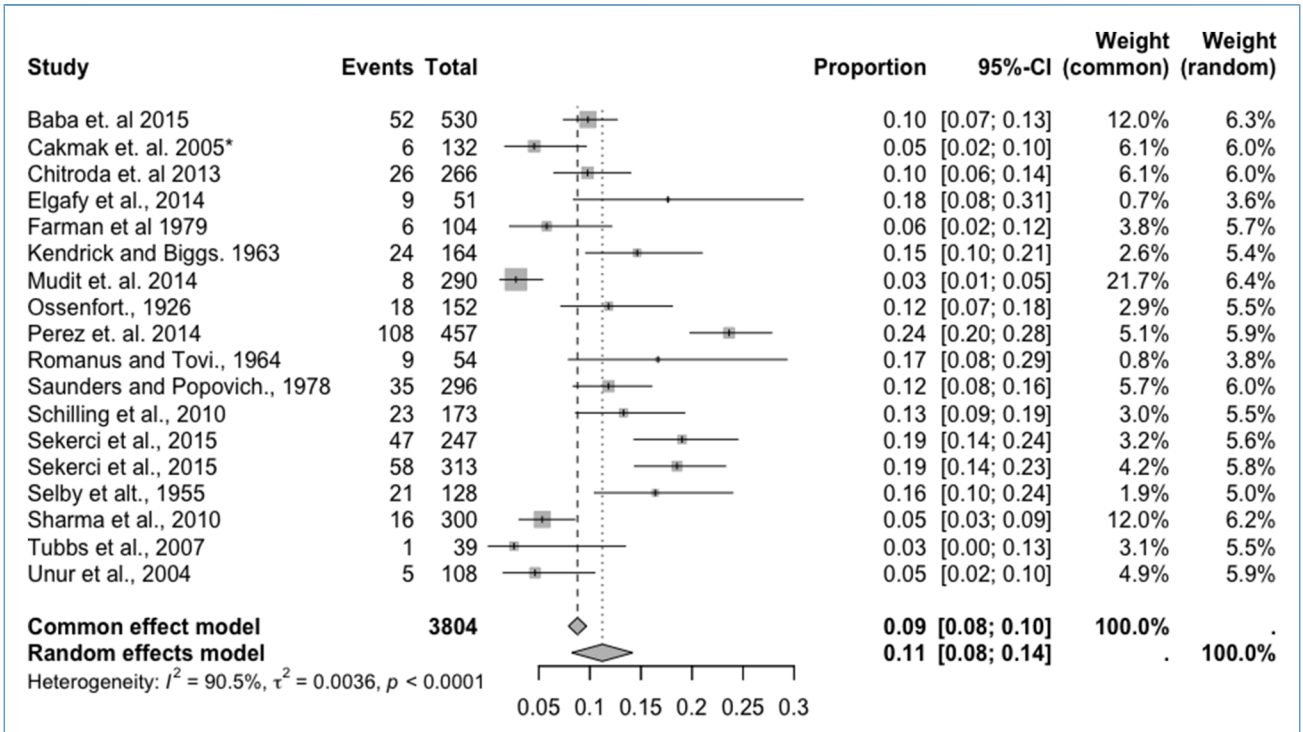

Figure 21. Forest plot prevalence studies male.

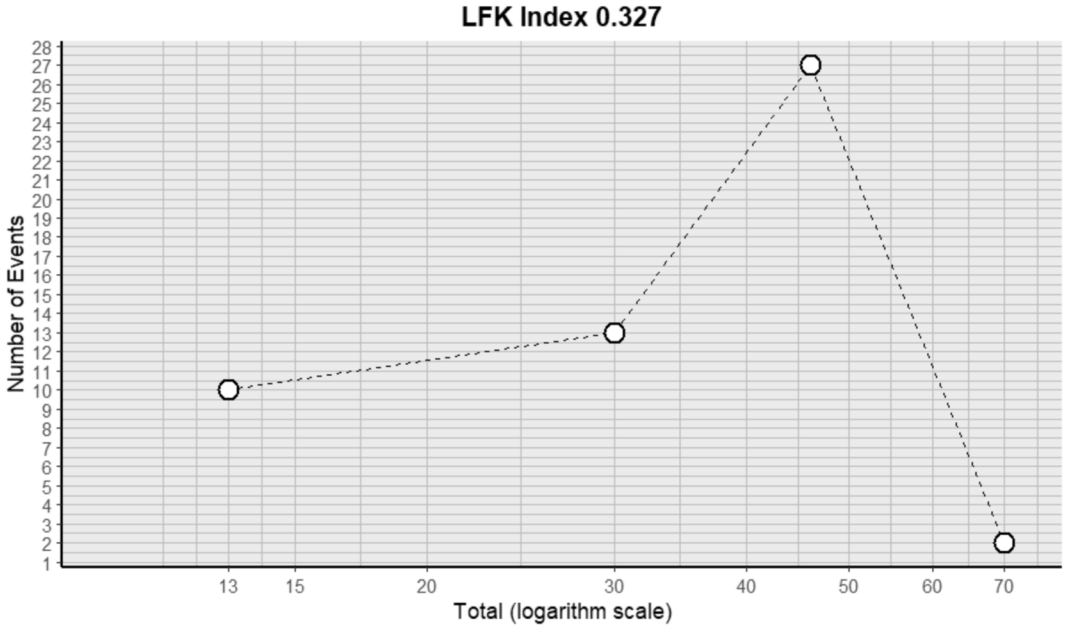

Figure 22. DOI plot prevalence studies male.

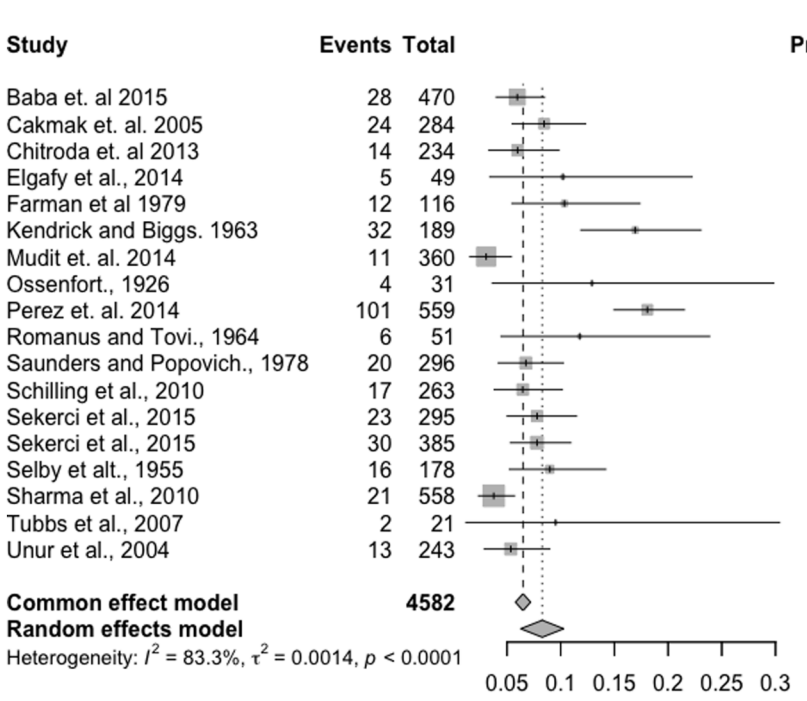

Figure 23. Forest plot prevalence studies female.

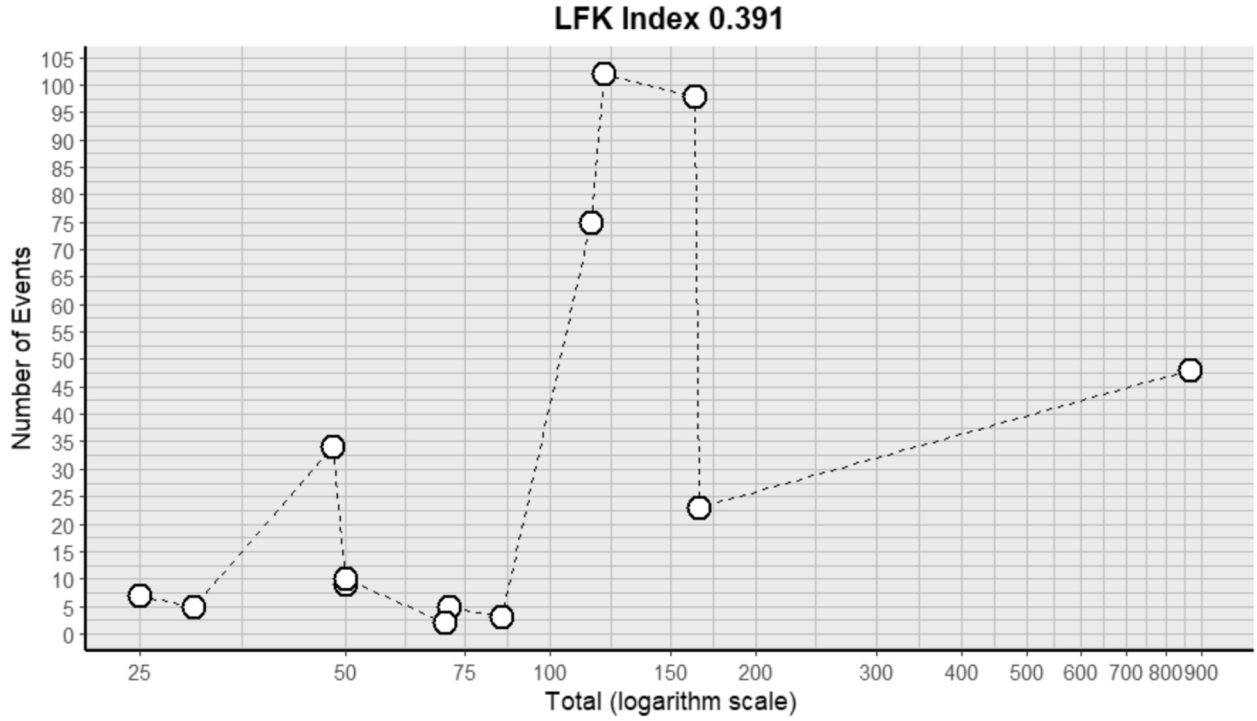

Figure 24. Doi plot prevalence studies female.

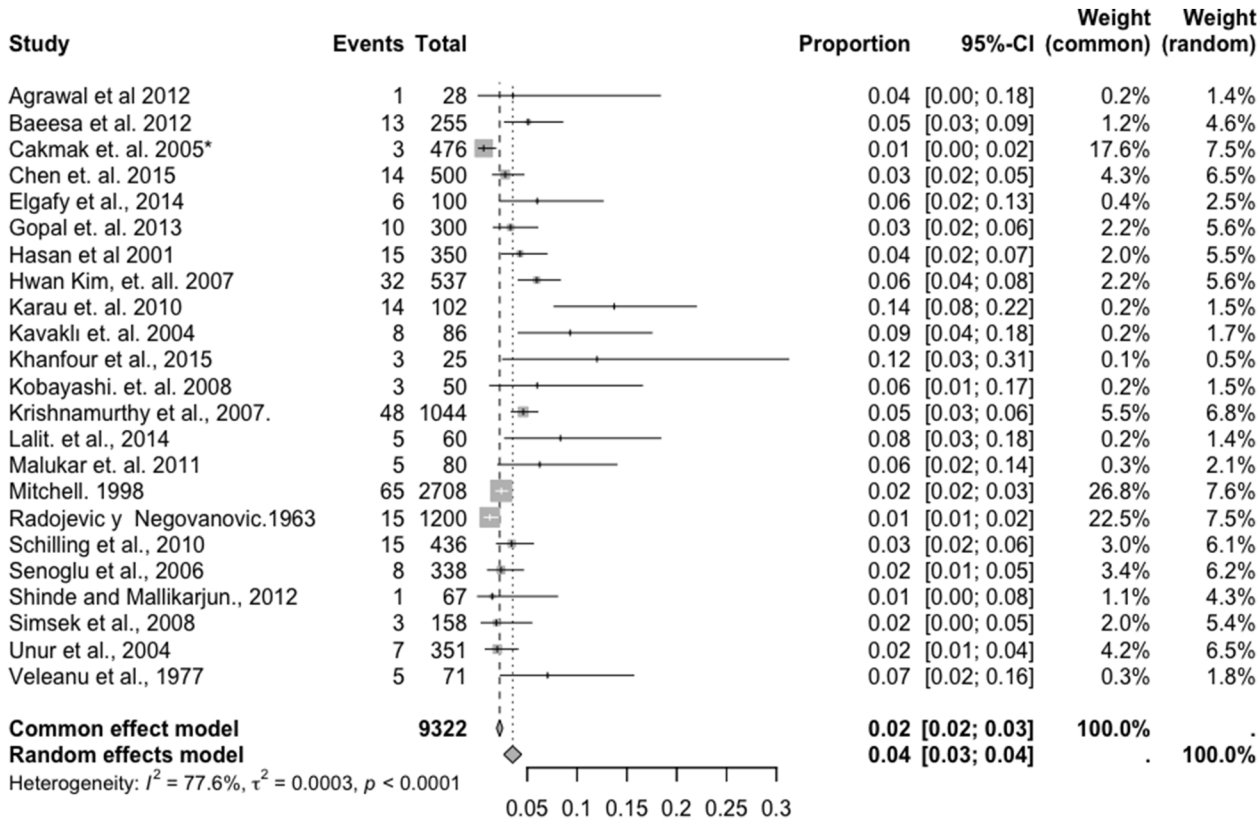

Figure 25. Forest plot prevalence of subjects with variant on the left side.

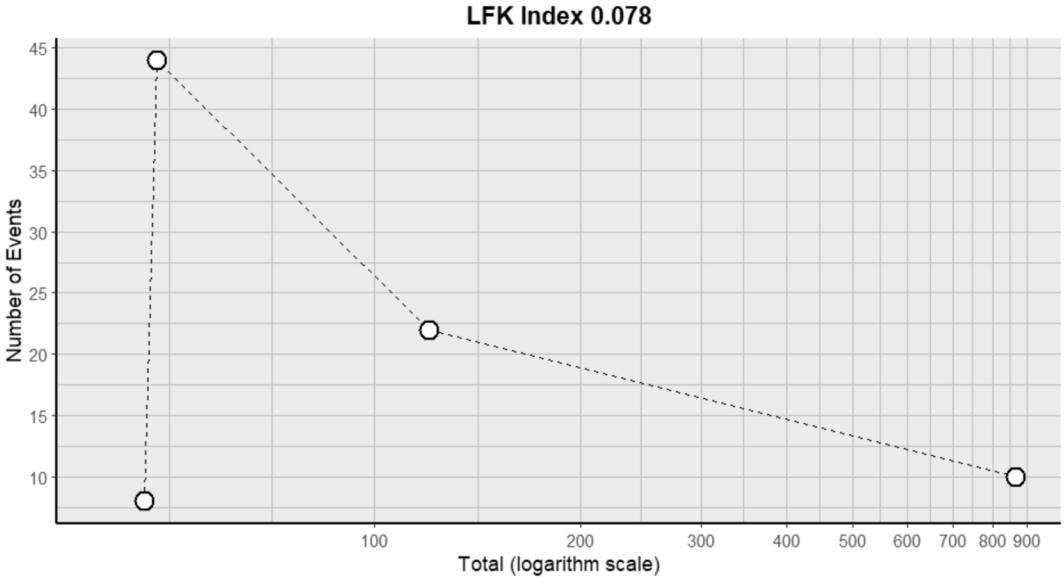

Figure 26. Doi plot prevalence of subjects with variant on the left side.

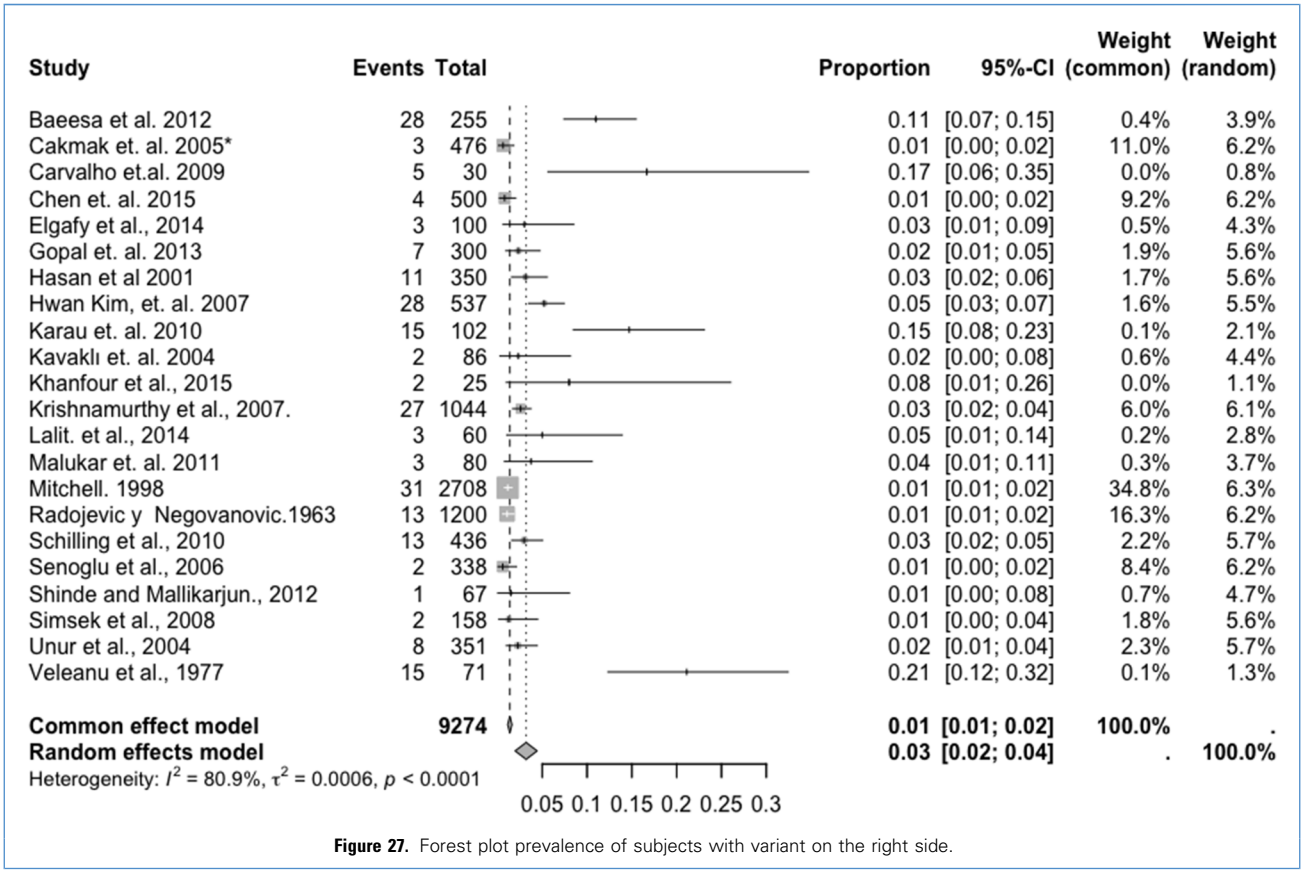

Figure 27. Forest plot prevalence of subjects with variant on the right side.

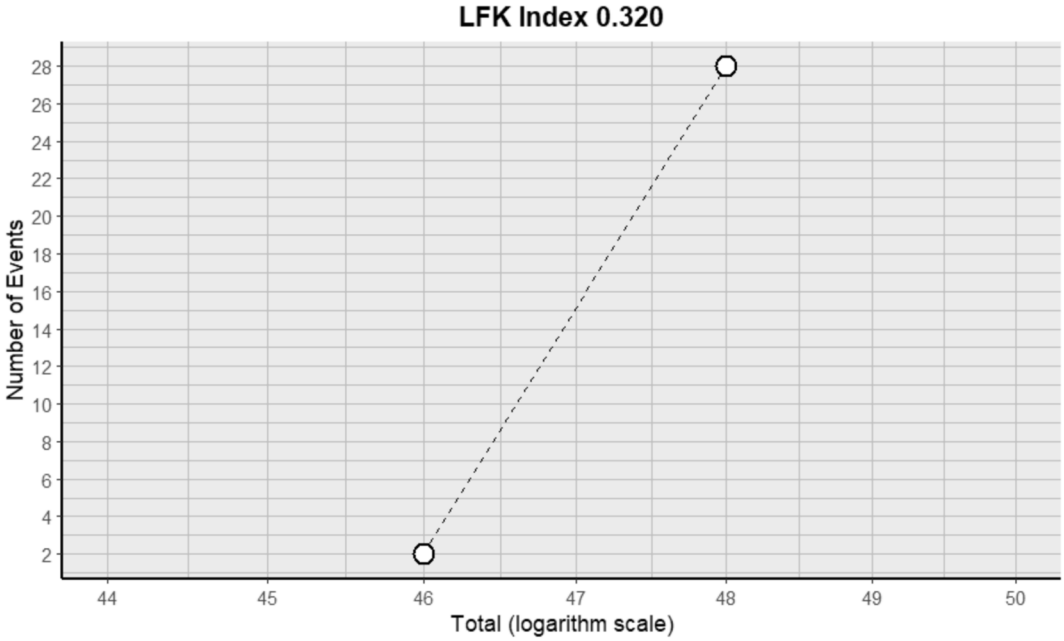

Figure 28. Doi plot prevalence of subjects with variant on the right side.

the possible relationship between AF and migraines.[62] Also, diverse neurological symptoms have been reported in patients with an AF, such as vertigo, visual alterations, nausea, tinnitus and headaches. Therefore, in cases where an apparent cause for the presence of these symptoms cannot be determined, the patient must be evaluated for the

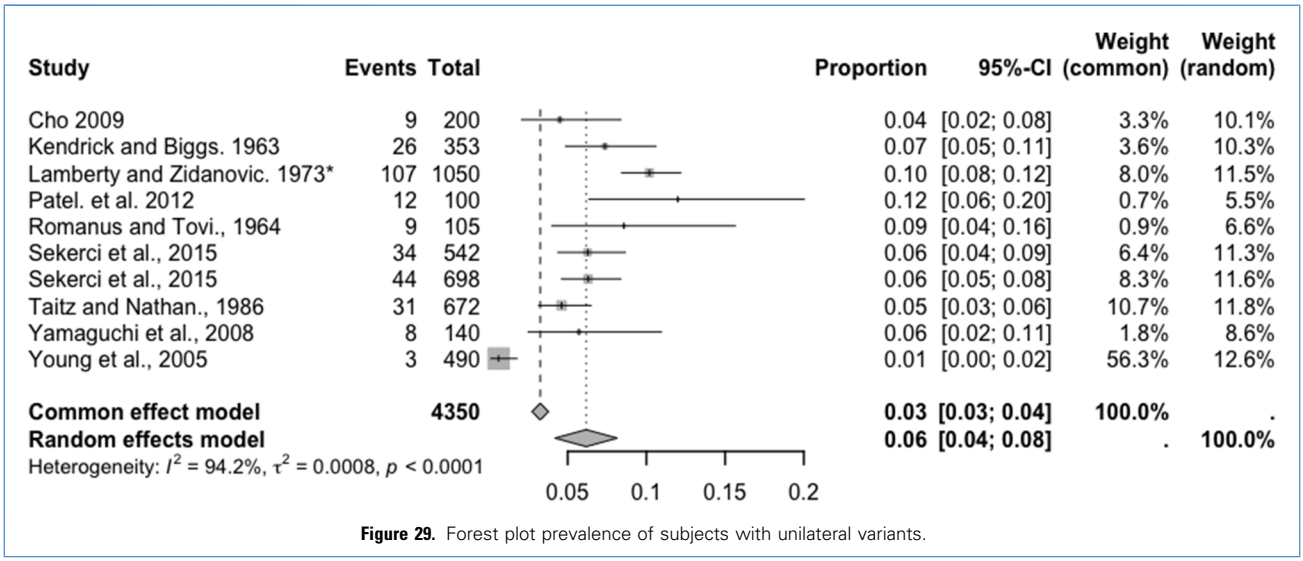

Figure 29. Forest plot prevalence of subjects with unilateral variants.

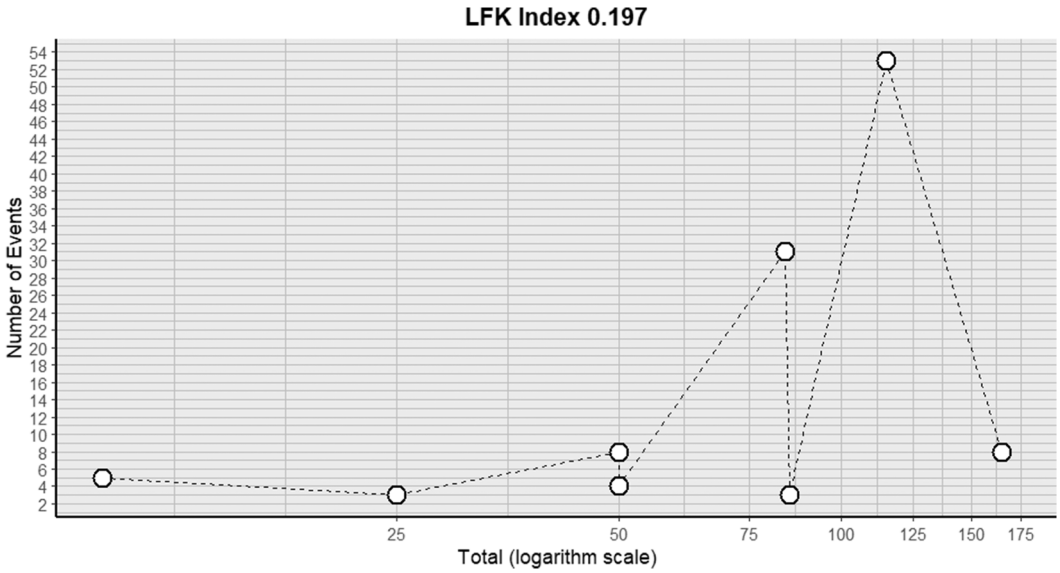

Figure 30. Doi plot prevalence of subjects with variant unilateral.

presence of an AF since, if they are found to have an AF, it is possible that surgical extraction of the foramen could improve their quality of life.[82-87]

The present study differentiates from previously published ones in providing the detailed anatomy of an AF and describing a larger cohort of clinical implications involved with its presence, highlighting the importance of knowing the anomaly and its implications. Of the 65 articles analyzed for this study, close to half of them come from the Asian continent, where India has the largest number with 16 publications. With the compiled data, however, it is not possible to establish a statistically significant association between the prevalence of an AF and a particular geographic region. Nor is it possible to correlate the presence of an AF and a specific sex group either. The obtained data comes mostly from radiological imaging studies, where the use of cephalometric radiographs is much more common than CT. Also, 31 of the studies reported the presence of an AF by the observation of bone remains in human donor material. One of the limitations of our study is that the study by Pekala et al., 2017, similarly addressed the prevalence of AF variants, our study focused differently on an aggregated approach to the neurosurgical clinical implications of the presence of AF, in addition our inclusion criteria were different from those of Pekala, ours being mainly the anatomical clinical relationship of the presence of AF, finally based on this study we have added 7 different studies that mainly added relevant clinical components for management in the presence of AF.

CONCLUSION

This review efficiently collected reliable AF data, with an emphasis on the different associated clinical presentations. It also demonstrated that the study of the anatomy of the AF and the way it presents in the population is important due to its great relevance as a diagnostic differential when facing different signs and symptoms with which this anatomical variation may be associated. These include but are not limited to headaches, vertigo, pain in the neck and shoulder area, Barré-Liéou syndrome, vertebrobasilar insufficiency syndrome and sensorineural hearing loss. This is mainly due to the compression it generates on the VA, the suboccipital nerve and the cervical venous plexus when rotating and/or laterally flexing the neck. Furthermore, the importance of considering its value in the pre-surgical approach to procedures involving the implementation of screws in the cervical region was also highlighted. The treatment of atlantoaxial instability is an example of this. A poor understanding of

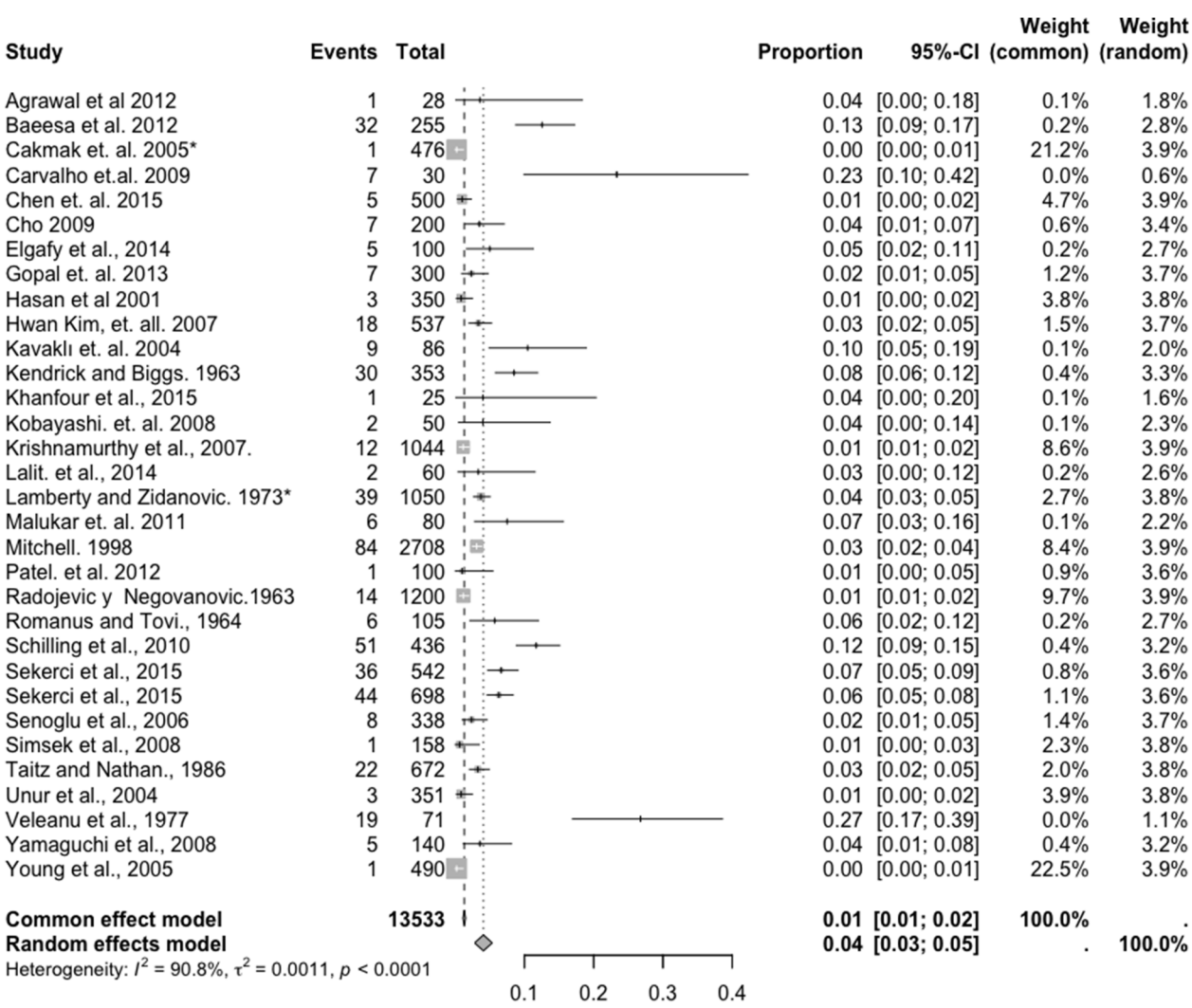

Figure 31. Forest plot prevalence of subjects with variant bilateral.

the patient's anatomy can lead to complications, such as VA injury and, consequently, compromised blood supply to the brain, cerebellum, and brainstem. For all these reasons, the authors encourage further research on this topic in other subgroups or in relation to other disciplines, in order to contribute to the knowledge of the AF and thus provide tools for healthcare professionals and other researchers, always in pursuit of improving people's lives.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Juan José Valenzuela-Fuenzalida: Visualization, Validation, Supervision, Resources, Methodology, Formal analysis, Conceptualization. **Javiera Cornejo-Peña:** Validation, Software, Methodology, Funding acquisition, Conceptualization. **Josefina Martinez-Cid:** Validation, Software, Project administration, Methodology, Conceptualization. **Cristobal Rojas-Acuña:** Validation, Methodology, Investigation, Data curation. **Guinevere Granite:** Writing — review & editing, Validation, Resources, Project administration. **Juan. A. Sanchis-Gimeno:** Supervision, Resources, Investigation, Funding acquisition, Data curation. **Alejandro Bruna Mejias:** Writing — original draft, Validation, Supervision, Resources, Methodology, Investigation, Data curation. **Pablo Nova Baeza:** Visualization, Validation, Resources, Methodology, Funding

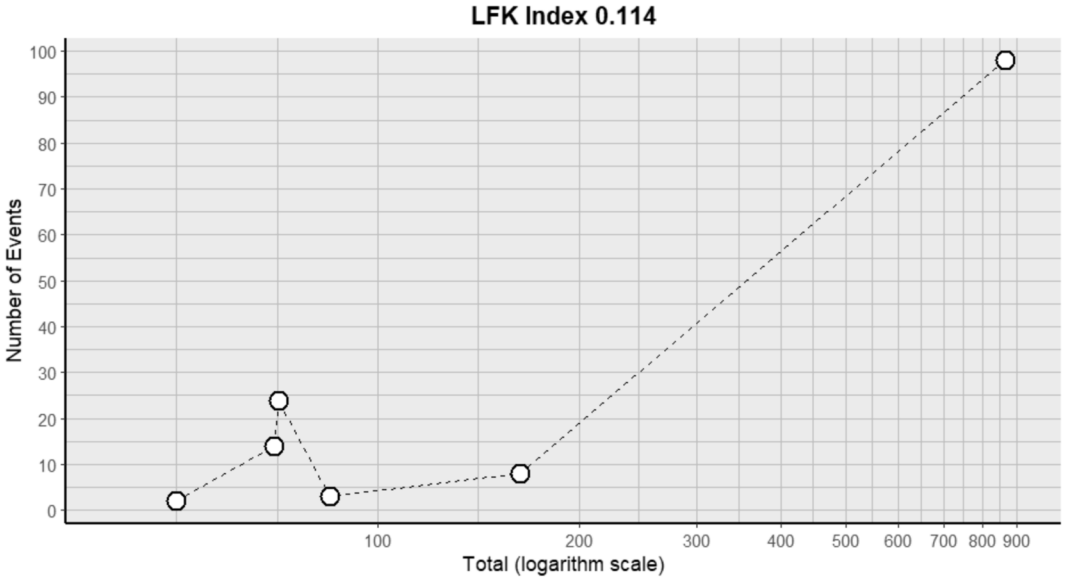

Figure 32. Doi plot prevalence of subjects with variant bilateral.

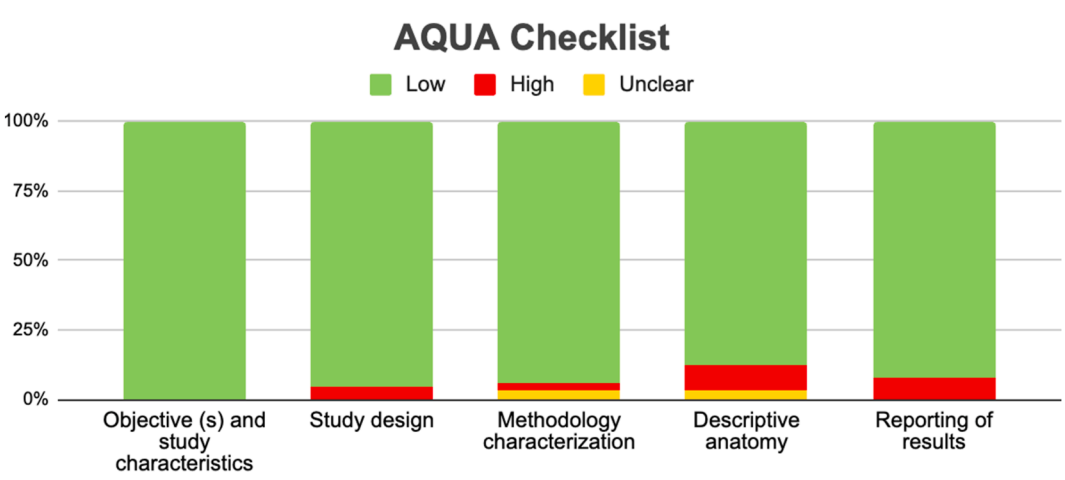

Figure 33. Risk of bias included studies.

acquisition, Data curation. **Mathias Orellana Donoso:** Writing — review & editing, Writing — original draft, Visualization, Methodology, Funding acquisition, Data curation. **Gustavo Oyanedel Amaro:** Visualization, Supervision, Software, Resources, Investigation, Data curation. **Macarena Rodriguez-Luengo:** Supervision, Resources, Methodology, Funding acquisition, Data curation. **Gkionoul Nteli Chatzioglou:** Supervision, Project administration, Investigation, Data curation. **Marko Konchaske:** Supervision, Project administration, Investigation, Formal analysis.

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