Cite as: Sibuor W, Kipkorir V, Cheruiyot I, Gwala F, Olabu B: Prevalence of femoral vein duplication: systematic review and metaanalysis. J Ultrason 2021; 21: e326–e331. doi: 10.15557/JoU.2021.0054.

Submitted: 12.05.2021
Accepted: 21.07.2021
Published: 29.11.2021

Prevalence of femoral vein duplication: systematic review and metaanalysis

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DOI: 10.15557/JoU.2021.0054

Keywords
femoral vein duplication, deep venous thrombosis, ultrasound

Abstract

Background: Duplication of the femoral vein is an important anatomical variation of the venous anatomy which has been shown to have an impact on the diagnosis of deep venous thrombosis by compression ultrasonography. The presence of duplication may result in false negative findings while evaluating for deep venous thrombosis, with serious consequences such as pulmonary embolism and death. This metaanalysis aims to determine the pooled prevalence of duplicated femoral veins. **Methods:** A systematic search was conducted through the major databases PubMed, Hinari, Embase and Medline to identify studies eligible for inclusion. Appropriate data were extracted and pooled into a random-effects metaanalysis using MetaXL software. The primary and secondary outcomes of the study included the pooled prevalence of duplicated femoral veins and the prevalence of bilaterally duplicated femoral veins, respectively. **Results:** A total of 11 studies (n = 3,682 limbs) were included. The overall pooled prevalence of duplicated femoral veins was 19.7% (95% CI 11–30). There was a significant difference in prevalence between cadaveric studies (2%, 95% CI 1–4) and imaging studies (25%, 95% CI 17–34). **Conclusion:** Duplication of the femoral vein is a common variation in the lower limbs. Routine watch-out should be practiced especially when performing lower limb Doppler studies in cases of deep venous thrombosis in order to avoid misdiagnosis and improve diagnostic accuracy.

Introduction

Femoral vein is the continuation of the popliteal vein beyond the adductor hiatus into the thigh. It ascends together with the femoral artery within the adductor canal and into the femoral triangle, where it is joined by the profunda femoris vein to form the common femoral vein. This terminates as the external iliac vein behind the inguinal ligament[1]. There are several variations in the anatomy of the deep venous system of the lower limb, one of such variations being duplication of the femoral veins.

The presence of duplicated femoral vein (DFV) is an important anatomical variation which has been shown to result in false negative compression ultrasound results during evaluation for deep venous thrombosis[2–4]. The ultrasound probe may be focused on one of the branches that does not have a thrombus, whereas the thrombus may be lodged in the other branches. This may result in misdiagnosis with serious consequences such as pulmonary embolism, post-thrombotic syndrome and death. It is therefore important to be wary of this variation in anatomy during ultrasonography.

Lower extremity deep venous thrombosis (DVT) is a common cause of morbidity and mortality, with a prevalence of 1 in 1,000 people and accounting for up to 100,000 deaths annually[5]. The most feared complication is pulmonary thromboembolism, when a thrombus becomes dislodged and travels to the pulmonary arteries. This may lead to sudden death if not diagnosed early[6]. Early diagnosis and intervention are, therefore, vital to prevent mortality. Lower extremity DVT is classified into proximal and distal DVT. Proximal DVT occurs in the deep veins above the knee (external iliac, femoral and popliteal), whereas distal DVT occurs in the deep veins below the knee without any involvement of the proximal veins[7,8]. Proximal extension of distal DVTs can be found in up to 15% of cases[9]. The proximal DVTs are more likely to dislodge and cause clinically significant morbidity and mortality[7]. Current guidelines from The

Society of Radiologists in Ultrasound recommend a comprehensive duplex ultrasound scan of all the lower limb veins from the thigh to the ankle when evaluating for DVT[10].

Contrast venography has historically been considered the gold standard for the diagnosis of DVT, but it is too invasive and hence less frequently used. As such, Doppler ultrasound is currently used as the standard first-line imaging modality for diagnosing DVT owing to its safety, reliability, accuracy, ease of access, and non-invasiveness[5,10,11]. Proximal lower extremity thrombi are commonly diagnosed by performing an ultrasound of the femoral-saphenous veins with compression. The diagnostic criteria for DVT by ultrasonography include incompressibility of a venous segment, lack of flow, visualization of thrombus, and abnormal spectral pattern[5,12]. Adequate knowledge of the normal and variant anatomy of the femoral vein is important in order to correctly identify the vein and make proper diagnosis. The presence of duplicated femoral veins has been reported before but the findings have been varied, with a prevalence ranging from 5–46%[4,13,14]. This metaanalysis, therefore, sets out to determine the pooled prevalence of duplicated femoral veins.

Methods

Study protocol and registration

This study was conducted in conformity with the Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[15]. The study protocol was registered on PROSPERO, an international prospective database for reviews developed by the University of York, Registration No. CRD42021223887.

Anatomic definitions considered

Duplication of the femoral vein was considered when a deep venous channel that was in contiguity with the femoral vessels communicated with the femoral vein or popliteal vein inferiorly and re-entered the femoral vein superiorly or had a common ending with the femoral vein. Isolated duplications of the popliteal veins or venae comitantes in the popliteal region extending proximally into the thigh were not considered.

Search strategy

A systematic search of the literature through 20th January 2021 was conducted on the electronic databases PubMed, Hinari, Embase and Medline to identify studies eligible for inclusion in the study. The search strategy used for PubMed is presented in Tab. 1. No language restriction was made. As for articles published by the same study group and also having an overlap of the search period, only the most recent article was included in order to avoid the duplication of data. The PubMed function "related articles" was used to extend the search, and a reference list of all the included studies was analyzed to identify any potentially eligible studies for inclusion. A search on Google Books was done for the analysis of the gray literature (https://books.google.com).

Tab. 1. *Search strategy for PubMed*

1.	(anatomy) OR (prevalence)
2.	(((double) OR (bifid)) OR (duplicated)) OR (duplication)
3.	((femoral vein) OR (sub-sartorial vein)) OR (superficial femoral vein)
4.	1 AND 2 AND 3

Selection criteria

All cadaveric or imaging studies reporting clear extractable data regarding the prevalence of DFV were included in the study. Review articles, case reports, letters to editors and papers with incomplete data were excluded. All the studies were assessed for eligibility by two independent reviewers (SW & VK), and any arising disagreements on eligibility were settled by consensus.

Data extraction and quality assessment

Data was extracted by two independent reviewers (WS & VK). The following information was extracted for each study: surname of the first author, year of publication, geographical region where the study was performed, type of study (cadaveric or imaging), sample size, prevalence of DFV, and bilaterality of duplication. Any disagreements during the extraction process were resolved by consensus. The risk of bias and quality assessment of all selected full-text articles was performed using the Anatomical Quality Assessment Tool (AQUA tool) from the International Evidence-Based Anatomy working group, Poland[16].

Outcomes

Primary outcome. The outcome of interest was the pooled prevalence of duplicated femoral veins.

Secondary outcomes. Prevalence of bilaterally duplicated femoral veins.

Metaanalytical synthesis methods

The analysis of the extracted data was performed using the MetaXl to calculate the pooled prevalence of DFV. DerSimonian-Laird model with a Freeman-Tukey double arcsine transformation was used to combine the summary data. A random-effects model was applied due to the high levels of heterogeneity displayed by anatomical data. The data reported here have been back transformed. The magnitude of heterogeneity among the included studies was assessed using the chi-squared test (Chi^2) and I-squared statistic (I^2). For the Chi^2 test, a Cochrane's Q p-value of <0.10 was considered significant. The values of the I^2

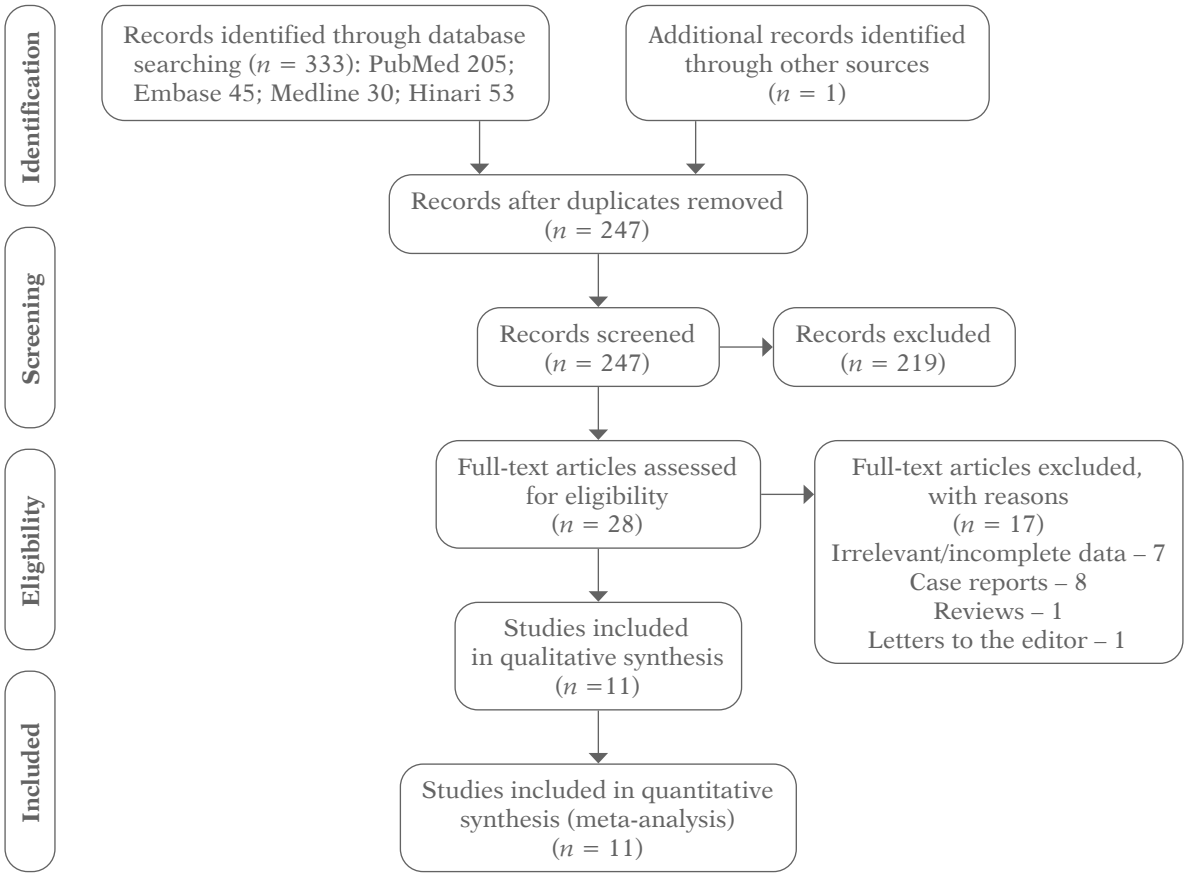

Fig. 1. *PRISMA flow diagram showing the study identification process*

statistic were interpreted as follows at a 95% confidence interval: 0–40% might not be important, 30–60% might indicate moderate heterogeneity, 50–90% may represent substantial heterogeneity, and 75–100% may represent significant heterogeneity. Subgroup analysis was performed based on the geographical regions from which the studies originated and the type of study (cadaveric or imaging). The imaging studies were further subjected to sub-group analysis for different imaging modalities (Multidetector-CT, Ultrasound, venography). Additionally, a leave-one-out sensitivity analysis was conducted to assess the robustness of the results and to further probe the sources of interstudy heterogeneity.

Results

Study identification

The initial search produced a total of 334 potentially relevant articles. Following the removal of duplicates and primary screening, 28 articles were assessed by full text for eligibility in the metaanalysis. Of these, 17 were excluded because the primary and secondary outcomes of these studies did not match those of this review. Ultimately, a total of 11 articles were included in this systematic review and metaanalysis (Fig. 1).

Characteristics of included studies

A total of 11 studies were included in the analysis. The publication dates ranged from 1996 to 2015. The majority of studies (9 studies, n = 3,320) were imaging studies, while the remaining 2 were cadaveric (n = 362). Most studies were performed in Europe (6 studies, n = 1,724). The remaining were performed in Australia (2 studies, n = 728), South America (2 studies, n = 340), and Asia (1 study, n = 890). Table 2 shows a summary of the included studies.

Quality assessment of included studies

The AQUA tool probes for the potential risk of bias in five study domains (objectives and subject characteristics; study design; methodology characterization; descriptive anatomy; and reporting of results). The risk of bias within each domain is normally categorized as "Low", "High", or "Unclear". Two of the included studies showed a high risk of bias in domain 3 (methodology characterization), mainly because the methods applied in them were not described in enough detail for them to be reproduced. Similarly, two of the included studies had a high risk of bias in domain 1 (objectives and subject characteristics). This was mainly due to the fact that the baseline demographic data were missing.

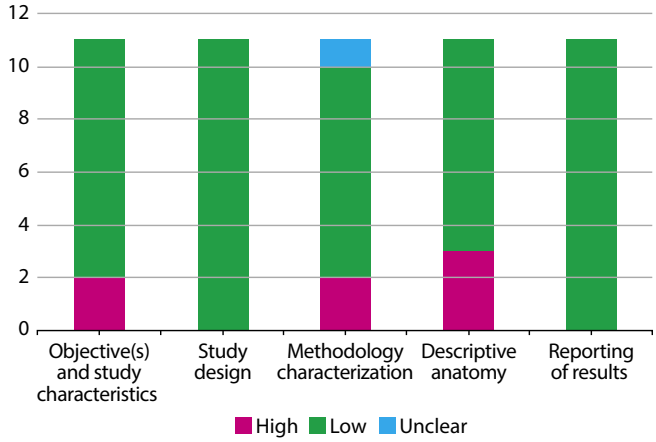

Fig. 2. *Bar graph summary of risk of bias assessment using the AQUA tool*

Three studies revealed a high risk of bias in domain 4 (descriptive anatomy) because the anatomical considerations were not described in enough detail. Most studies revealed the remaining domains (study design and reporting of results) to be at a low risk of bias (Fig. 2).

Prevalence of femoral vein duplication

Among the 11 included studies (n = 3,682), the pooled prevalence of DFV was 19.7% (95% CI 11.1–30.1). The interstudy heterogeneity for this outcome was high (I^2 = 98%). Fig. 3 is a forest plot summarizing the pooled prevalence. Subgroup analysis based on the study type revealed a significantly lower pooled prevalence in the cadaveric study group (pooled prevalence = 2%, 95% CI 1–4, I^2 = 0%) compared to the imaging studies (pooled prevalence = 25%, 95% CI 17–34, I^2 = 96%). Further subgroup analysis of the imaging studies revealed a significantly higher prevalence in the venography (35%, 95% CI 27–43, I^2 = 86%) and ultrasonography subgroup (33%, 95% CI 16–52, I^2 = 97%). The pooled prevalence was significantly lower in the multidetector CT (MDCT) subgroup (6%, 95% CI 0–19, I^2 = 97%). Table 3 presents a summary of the subgroup analysis.

The pooled prevalence of DFV was lower in the European studies (14%, 95% CI 2–30, I^2 = 98%) than in other regions (Australia = 27%, 95% CI 3–57; South America = 26%, 95% CI 0–91).

With regards to the bilaterality of duplication, only 5 studies reported this finding. The pooled prevalence was 15.9% (95% CI 6–28) with a high interstudy heterogeneity (I^2= 95.6%).

Discussion

This metaanalysis demonstrated that the pooled prevalence of DFV was high at 19.7%, with significant interstudy heterogeneity present. The heterogeneity could partially be explained by the difference in the modalities used in the evaluation of double femoral vein. For instance, ultrasonography is highly operator-dependent, and accurate interpretation relies on well-trained operators and techniques used[26]. This could potentially account for the high prevalence observed in the ultrasonography group. The significantly lower prevalence in the MDCT group (6%) can be explained by the patient characteristics in two of the three studies. The study subjects in the two studies by Bastarrika *et al.*, 2007[17] and Redondo *et al.*, 2009[23] had Klippel–Trénaunay syndrome, which is a congenital vascular anomaly associated with aplasia or hypoplasia of the deep venous systems. For instance, 50% of the patients included in the study by Bastarrika *et al.*, 2007[17] either had aplasia or hypoplasia involving the femoral vein, hence the low prevalence of duplication. The cadaveric studies may be a reflection of the true prevalence of duplicated femoral veins since they are based on thorough explorative evaluation. However, only two cadaveric studies were included in the study and the sample size was limited in one of them.

Clinicians need to be wary of the presence of DFV, as it could potentially impact on the diagnostic accuracy of compression ultrasonography when evaluating for DVT in the lower limbs. There is a possibility of failure to identify the clot in one arm of the double vein if the arm being evaluated has no clots, resulting in false-negative results[3,4]. Using venography, Streaton *et al.*, 1998[2], showed that it

Tab. 2. *Summary of the characteristics of included studies*

Author	Country	Region	Study type	Sample size	Duplicated femoral veins
Bastarrika, 2007[17]	Spain	Europe	Imaging (MDCT)	32	1
Casella, 2010[18]	Brazil	South America	Imaging (duplex)	314	173
Dona, 2000[3]	Australia	Australia	Imaging (duplex)	248	37
Gordon, 1996[19]	U.K.	Europe	Imaging (duplex)	116	29
Paraskevas, 2011[20]	Australia	Australia	Imaging (Sonography)	480	200
Park, 2011[21]	Korea	Asia	Imaging (MDCT)	890	214
Quinlan, 2003[22]	Denmark, U.K.	Europe	Imaging (venography)	808	253
Redondo, 2009[23]	Spain	Europe	Imaging (MDCT)	51	1
Screaton,1998[2]	England	Europe	Imaging (venography)	381	149
Uhl, 2010[24]	France	Europe	Cadaveric	336	7
Ferreira, 2015[25]	Colombia	South America	Cadaveric	26	1

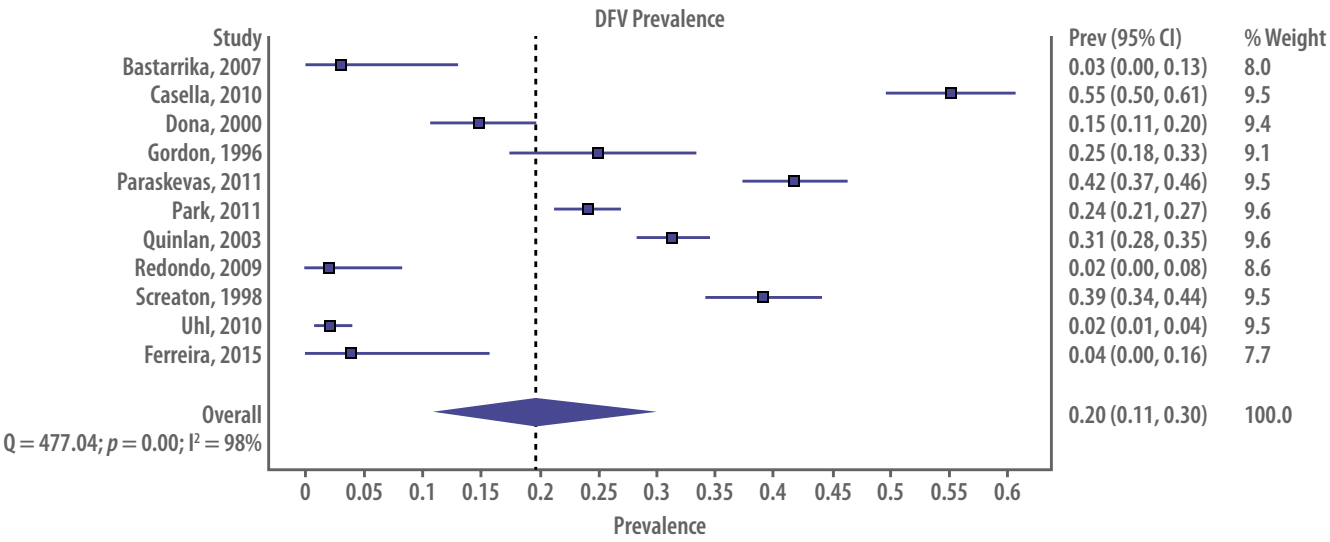

Fig. 3. *Forest plot showing the pooled prevalence of duplicated femoral veins*

was more likely to get a false negative femoropopliteal thrombosis on ultrasonography in cases of DFV compared to single veins. This observation was, however, not statistically significant. There is also a possibility of clinically silent DVTs without complete occlusion since there are collateral vessels[13]. A good proportion of these silent DVTs remain undiagnosed and may result in pulmonary embolism and death[27].

It is also postulated that duplication of the vein potentially results in an overall reduction in the velocity of blood flow along the duplicated veins, although this hypothesis has not been proven. Dona *et al*., 2010[3] established that femoral vein duplication resulted in an overall increase in venous cross-sectional area by about 42% compared to non-duplicated veins. They calculated a mean decrease in venous flow velocity by about 36%, with the assumption that venous flow rate must remain constant. This reduction in velocity could contribute to relative stasis, which could potentially predispose to DVT formation compared to non-duplicated veins.

The superficial femoral vein is also widely used as an arterial or venous vascular graft. Its applications include the repair of conventional infected grafts of mycotic aneurysms, aortoiliac reconstruction in occlusive arterial disease, and as a peripheral bypass material[28,29]. Segments of about 5–9 mm in diameter can be used as internal iliac grafts[18,30]. In this systematic review, 4 studies reported the mean diameters of DFV. Dona *et al*., 2000 (mean diameter of 7.2 mm) Fereira, 2015 (20 mm), Casella (25.4% of duplicates had diameters greater than 6 mm) and Gordon (4.9 mm)[3,18,19,25]. Except for the findings by Gordon *et al*.[19], duplicated femoral veins can be used successfully as vascular grafts given the adequacy of their diameters, conferring an advantage in these cases.

From the studies analyzed, only 5 reported on the bilaterality of occurrence of duplicated femoral vein, with a pooled prevalence of 15.9%. This could be a pointer to the occurrence of duplications in the contralateral limb in cases where clinical imaging detects duplication in one limb.

This study was limited by the small number of available studies on the prevalence of double femoral vein, and by the persistently high interstudy heterogeneity despite subgroup analysis. However, it still provides a comprehensive metaanalysis and systematic review on the currently available data on the prevalence of duplicated femoral vein.

Tab. 3. *Table showing a summary of subgroup analysis by region and study type*

Subgroup	Number of studies (number of limbs)	Pooled prevalence (LCI-HCI)	I²
Overall	11 (3682)	19.7% (11–30%)	98%
Imaging studies	9 (3320)	25% (17–34%)	96%
Cadaveric studies	2 (362)	2% (1–4%)	0%
South America	2 (340)	26.3% (0–91%)	97%
Asia	1 (890)	24% (21–27%)	N/A
Australia	2 (728)	27% (3–57%)	98%
Europe	6 (1724)	14% (2–30%)	98%
LCI – lower confidence interval; HCI – higher confidence interval; N/A – not applicable			

Conclusion

Duplication of the femoral vein is a common variation in the lower limbs. Routine watch-out should be practiced especially when performing lower limb Doppler ultrasound studies in cases of DVT in order to avoid misdiagnosis and improve diagnostic accuracy.

Conflict of interest

The authors have no conflicts of interest to declare.

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