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Understanding Spatial Relationship of Saphenous Nerve and Great Saphenous Vein in the Lower Leg Region: A Systematic Review and Meta-analysis

Comprensión de la Relación Espacial Entre el Nervio Safeno y la Vena Safena Magna en la Región de la Pierna: Una Revisión Sistemática y Meta-análisis

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SUMMARY: The anatomical relationship between saphenous nerve (SN) and the great saphenous vein (GSV) should be taken into account to avoid injuries to the SN during surgical harvesting of the GSV. The relationship of SN with GSV is highly variable in the lower leg region and there is no comprehensive dataset available on the positioning and distance of the SN with GSV in the lower leg region. The main goal of our study was to analyze the positioning and distance of GSV with SN in the lower leg region. A systematic literature search using PRISMA guidelines was performed in databases such as MEDLINE, PubMed, SciELO, and Cochrane reviews using search terms such as "Saphenous nerve" "Great saphenous vein" "distance" AND "lower leg region", which yielded 1248 article links. Of the fourteen studies that met the inclusion criteria comprising 592 lower limbs are in a range of 26-101 years age. Our pooled analysis revealed that the distance of SN with GSV in the lower third of the leg using a random effects model with Hartung-Knapp adjustment was 0.27 cm (95 % CI; τ^2=0.0049), indicating a relatively consistent anatomical proximity between these two structures. However, substantial heterogeneity was observed among the studies (I^2 = 97.6%, Q=254.3, $p < 0.0001$), suggesting significant variability in the reported distances. With regards to positioning of the SN with GSV, pooled estimate of our study revealed that the SN lies anterior to GSV in 31.4% cases, and in 33.1 % cases posterior to it. The predominance of SN lying deep to GSV aligns with 35.5 %, reflecting vulnerability of SN in surgical interventions of the GSV. Our data gives more representative values on the spatial relationship of SN with GSV in the lower leg region, and this information would be of great advantage for surgeons to avoid injury to the SN which can lead to sensory disturbances in the lower leg region and even the SN neuroma.

KEY WORDS: Great saphenous vein; Saphenous nerve; Distance; Lower leg region; Injury.

INTRODUCTION

The ankle region, which is highly mobile and unique in its anatomy for holding a hinge synovial joint that is formed by the articulation of the talus, tibia, and fibula bones. The lateral and medial malleoli form the lateral and medial borders; respectively (Manganaro & Alsayouri, 2023) and these malleoli houses many important structures such as arterial, venous and neural networks. Therefore, surgical procedures in this region should be meticulous for achieving successful outcomes by avoiding injuries to these structures (Carvallo & del Sol, 2011). In ankle surgeries, more than general anesthesia, regional nerve blocks shown to have positive outcomes by reducing the procedural errors and post-operative pain (Vadivelu *et al*., 2015). One such important nerve which needs special attention in ankle region is the saphenous nerve (SN). Classical anatomy textbooks have different opinions on the course of SN at the ankle level when compared with surgical orthopedics books and some of the surgical textbooks did not even describe the distal course of SN, despite being important in surgical practice (Hoppenfeld & DeBoer, 2003). Most of the classical anatomy textbooks described SN as the longest cutaneous branch of the femoral nerve (FN). After taking its origin from FN in the femoral triangle, it takes a lateral to medial course while descending to the adductor canal. The SN pierces the sartorial fascia above the medial aspect of the knee to become subcutaneous. It then gives rise to the infrapatellar branch that supplies the skin of the antero-inferior aspect of the knee. The SN below knee follows the same course with the greater

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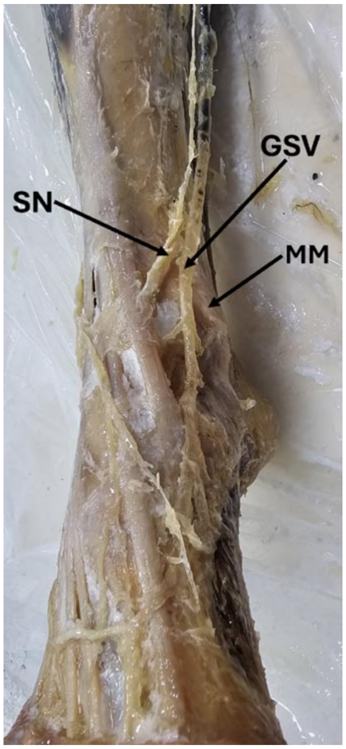

Fig.1. Anatomical dissection shows the course of saphenous nerve and great saphenous vein in the lower leg region at the level of medial malleolus. SN: saphenous nerve, GSV: great saphenous vein, MM: medial malleolus.

saphenous vein (GSV) to the medial aspect of the ankle and foot to terminate at the medial aspect of the head of the first metatarsal (Standring & Gray, 2008).

At the ankle, SN course appears to be very vague as per different descriptions (Mercer *et al*., 2011) and no standard dataset is available on its relationship with GSV. Some studies reported that the SN is located anterior to GSV (Fig. 1 & Fig. 2a) while others argued this and presented a few cases showing SN located posterior to the GSV (Fig. 2b) and in many cases, SN and GSV are inseparable and ensheathed by common fascia (Clendenen & Whalen, 2013; Dayan *et al*., 2008). Studies also reported that the standard dataset on SN's relationship with GSV is highly warranted for avoiding injuries to SN and GSV in ankle surgeries, particularly during the procedures of distal interlocking screws for tibial intramedullary nails (Mercer *et al*., 2011), regional anesthetic procedures involving SN block (Clendenen & Whalen, 2013) and while harvesting GSV for coronary artery bypass graft procedures (Mountney & Wilkinson, 1999), lower leg is the routinely used area for harvesting the GSV due to the similarities in the diameter of GSV with the coronary arteries (Durko *et al*., 2018), and the current guidelines of the European Society for Vascular Surgery proposed that the availability of an autologous GSV conduit is vital for a successful bypass surgery (Golovina *et al*., 2024). Therefore, keeping the importance of neurovascular structures of the lower leg in mind, we conducted a thorough search on the anatomical relationship of SN and GSV to derive a standard dataset on their distance and anatomical relationship which might help vascular surgeons to avoid their injury during harvesting procedures.

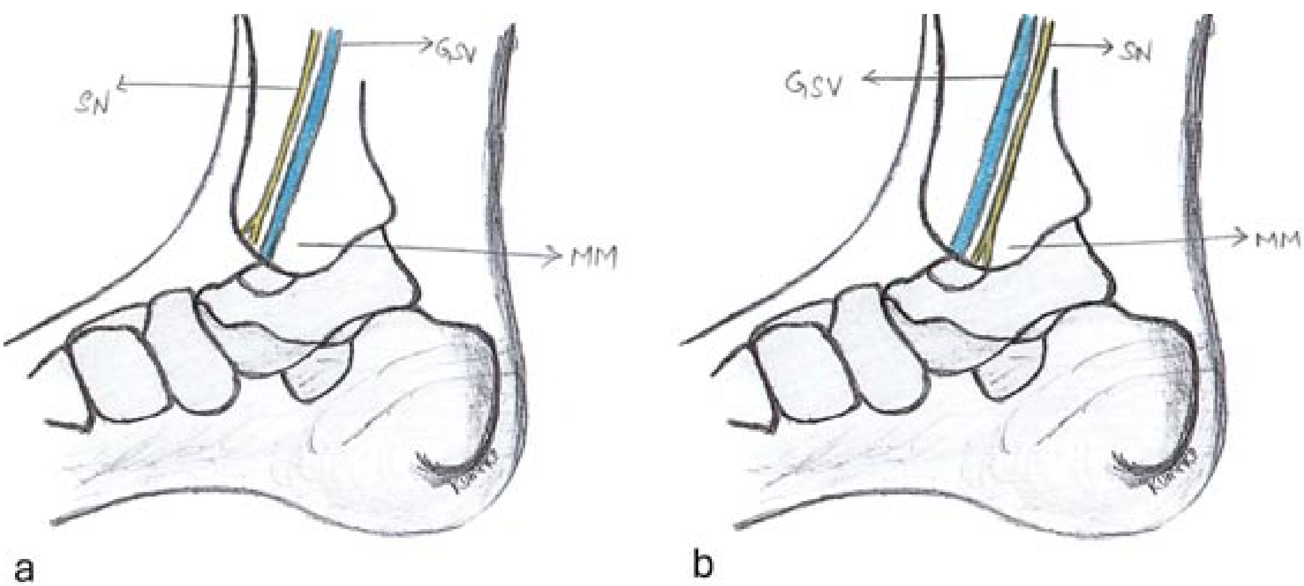

Fig.2a. Schema showing the saphenous nerve passing anterior to the great saphenous vein. Fig.2b. Schema showing the saphenous nerve passing posterior to the great saphenous vein. SN: saphenous nerve, GSV: great saphenous vein, MM: medial malleolus.

MATERIAL AND METHOD

Literature search strategy & inclusion-exclusion criteria

A thorough literature search was conducted mainly using electronic databases such as MEDLINE, PubMed, SciELO, and Cochrane reviews. The keywords used for search were "Great saphenous vein" "Saphenous nerve" "distance" AND "lower leg region". To arrive at a standard dataset of this surgically important area, we have strictly confined our search criteria to the cadaveric studies by excluding all case reports, case series, letters to editor, brief communications and studies that did not meet keywords of our search. The mean pooled data on the relationship and distances of GSV with SN in the lower leg region were set to be the outcome of our study. The references of the studies included were thoroughly checked, and duplicates were removed. No restrictions were set on the date and language of the studies. The titles and abstracts of the articles were initially screened to obtain the full-text of articles (Fig. 3). The guidelines of Preferred Reporting Items for Systematic reviews and MetaAnalyses (PRISMA) were used in collecting our data (Moher *et al*., 2009). This study was conducted upon obtaining necessary permissions from the Research & Ethics Committee (REC) of College of Medicine & Health Sciences, Arabian Gulf University (Reference no: E23-PI-04-25).

Statistical analysis. A systematic review and meta-analysis were conducted to evaluate the spatial relationship between GSV and SN in the lower leg. For continuous outcomes (GSV-SN distance), the weighted mean difference (WMD) with 95 % confidence intervals (CI) was calculated using the inverse variance method. For proportional outcomes (positional relationships), proportions were transformed using the Freeman-Tukey double arcsine transformation to stabilize variances before pooling. All effect sizes were synthesized under the random-effects model with Hartung-Knapp adjustment was applied to account for anticipated clinical and methodological heterogeneity. Heterogeneity was quantified using I^2 statistics and τ^2 (tau-squared), with values greater than 75 % considered substantial with prediction intervals calculated to assess clinical generalizability. All analyses were conducted in R 4.3.2 with the meta package, metafor for advanced modeling, dmetar for clinical interpretation, and forest plot for visualization. Statistical significance was set at α=0.05 and all analyses adhered to PRISMA guidelines for systematic reviews and meta-analyses.

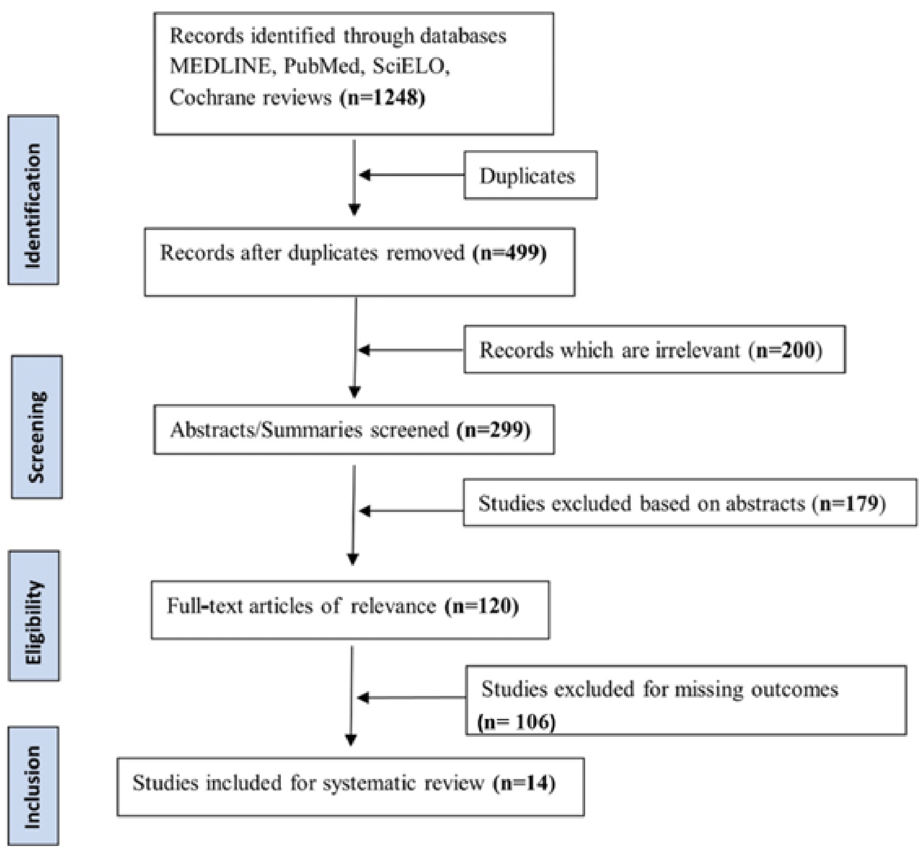

Fig.3. Showing the application of selection criteria as per PRISMA guidelines.

RESULTS

Studies included. A total of 14 studies including 592 lower limbs with a sample of 227 right, 230 left and 135 unspecified lower limbs met the study criteria (Fig. 3 & Table I). Although abstracts of 299 studies were initially screened, only a small portion of them (n=14; 4.68% of studies) were included in our analyses because most of the studies did not report the data on keywords of our study. The specimens are in a range of 26-101 years age. Eight studies (Murakami *et al*., 1994; Ozsoy *et al*., 2009; Woo *et al*., 2010; Wilmot & Evans., 2013; Tothonglor *et al*., 2013; Tonogai *et al*., 2018; Warehime *et al*., 2013; Peng *et al*., 2024) reported their sex distribution with 238 male and 138 female lower limbs. Six studies have not reported data on their sides and gender (Table II). Tables I, II and III show the characteristics of included studies and outcomes of individual studies.

Positional variations of SN and GSV in the lower leg region. Eleven studies did not report the relationship between SN and GSV (Table III). Three studies comprising 138 limbs have reported the relationship between SN and GSV from three different populations (Table III). Pooled analysis revealed anterior (31.4 %), posterior (33.1 %), and deep (35.5%) relationships across 138 limbs, with extreme heterogeneity (I^2>90 %) indicating anatomical variability. Our pooled data on the population revealed that the sample from the Czech Republic revealed 57.7 % cases, wherein, SN is located anterior to the GSV (Fig. 2a), while 42.3 % posterior to the GSV (Fig. 2b) (Veverkova *et al*., 2011). Another study from the Caribbean region revealed a different scenario of SN located anterior to the GSV in 14.28 % cases with SN crossing the GSV antero-posteriorly (Fig. 4a) in 35.72 % cases and from the posterior-to-anterior aspect (Fig. 4b) in 50 % cases (Ghosh & Chaudhury, 2019). Another study from Canadian population presented 22 % each of SN located anterior and posterior to the GSV while 56 % cases deep to the GSV (Peng *et al*., 2024). The predominance of deep relationships (56 %) in Peng *et al*. (2024), aligns with the pooled estimate of 35.5 % (0.0-78.2 %), reflecting vulnerability of SN in surgical interventions of GSV (Table IV). Apparent differences between study-specific

Table I. Studies included in our search.

Serial number	Authors	Country	Year	Study type	Procedure
1	Murakami *et al*.	Japan	1994	Cadaveric	Dissection
2	Ozsoy *et al*.	Turkey	2009	Cadaveric	Dissection
3	Woo *et al*.	Hongkong	2010	Cadaveric	Dissection
4	Veverkova *et al*.	Czech Republic.	2011	Cadaveric	Dissection
5	Wilmot & Evans	United Kingdom	2013	Cadaveric	Dissection
6	Tothonglor *et al*.	Thailand	2013	Cadaveric	Dissection
7	Jeon *et al*.	South Korea	2018	Cadaveric	Dissection
8	Tonogai *et al*.	Japan	2018	Cadaveric	Dissection
9	Ghosh & Chaudhury	Saint Kitts and Nevis	2019	Cadaveric	Dissection
10	Gohiya *et al*.	India	2020	Cadaveric	Dissection
11	Lehtonen *et al*.	NR	2020	Cadaveric	Dissection
12	Warehime *et al*.	USA	2023	Cadaveric	Dissection
13	Peng *et al*.	Canada	2024	Cadaveric	Dissection
14	Sakkab *et al*.	USA	2024	Cadaveric	Dissection

NR = not reported.

Table II. Characteristics of the included studies.

Serial number	Authors	Year	Sample size of limbs	Side of the limbs		Sex		Age range (mean)
				Right	Left	Male	Female	
1	Murakami *et al*.	1994	148	74	74	120	28	27 to 94 (NR)
2	Ozsoy *et al*.	2009	31	NR	NR	19	12	35 to 80 (59.0)
3	Woo *et al*.	2010	23	12	11	8	15	53 to 88 (68.0)
4	Veverkova *et al*.	2011	86	43	43	NR	NR	NR
5	Wilmot & Evans	2013	37	19	18	15	22	50 to 101 (82.4)
6	Tothonglor *et al*.	2013	95	48	47	62	33	26 to 93 (70.5)
7	Jeon *et al*.	2018	38	NR	NR	NR	NR	43 to 92 (62.3)
8	Tonogai *et al*.	2018	6	0	6	3	3	70 to 100 (81.5)
9	Ghosh & Chaudhury	2019	42	21	21	NR	NR	NR
10	Gohiya *et al*.	2020	20	NR	NR	NR	NR	NR
11	Lehtonen *et al*.	2020	10	NR	NR	NR	NR	(78.2)
12	Warehime *et al*.	2023	20	10	10	0	20	65 to 92 (85.5)
13	Peng *et al*.	2024	10	NR	NR	5	5	(79.2)
14	Sakkab *et al*.	2024	26	NR	NR	NR	NR	NR

NR = not reported

percentages and pooled estimates arise from inverse-variance weighting and heterogeneity adjustment, where smaller studies (Ghosh & Chaudhury, 2019) contribute proportionally less than larger studies (Veverkova *et al*., 2011).

Table III. Summarizing the distance and relation of SN with GSV.

Serial Number	Authors	Year	Relation of SN with GSV (%)	Distance between SN and GSV (cm) Right	Left
1	Murakami *et al.*	1994	NR	NR	NR
2	Ozsoy *et al.*	2009	NR	NR	NR
3	Woo *et al.*	2010	NR	NR	NR
4	Veverkova *et al.*	2011	In 57.7% cases anterior to GSV In 42.3% cases posterior to GSV	0.26 (sides were not specified)	
5	Wilmot & Evans	2013	NR	NR	NR
6	Tothonglor *et al.*	2013	NR	NR	NR
7	Jeon *et al.*	2018	NR	0.2 (sides were not specified)	
8	Tonogai *et al.*	2018	NR	NR	0.27 when plantarflexed 0.31 when dorsiflexed
9	Ghosh & Chaudhury	2019	In 14.28 % cases anterior to GSV In 35.72 % cases SN crossed GSV from anterior to posterior In 50% cases SN crossed GSV from posterior to anterior	NR	NR
10	Gohiya *et al.*	2020	NR	0.38 (sides were not specified)	
11	Lehtonen *et al.*	2020	NR	0.26 (sides were not specified)	
12	Warehime *et al.*	2023	NR	0.23	0.32
13	Peng *et al.*	2024	22 % anterior to GSV 22 % posterior to GSV 56 % deep to the GSV	NR	NR
14	Sakkab *et al.*	2024	NR	0.16 (sides were not specified)	

SN = saphenous nerve; GSV = great saphenous vein; NR= not reported.

Table IV. Meta-analysis of the spatial relationship between SN and GSV.

Parameter	Studies (n)	Limbs (n)	Pooled Estimate (95 % CI)	I^2 (95 % CI)	τ^2	Prediction Interval
Distance of SN with GSV (cm)	7	163	0.27 % (0.21-0.29 %)	92.3 % (89-96 %)	0.0049	0.15-0.35
Anterior position of SN with GSV	3	138	31.4 % (4.6-58.2 %)	95.7 % (92-99 %)	0.081	0.0-78.5
Posterior position of SN with GSV	3	138	33.1 % (8.9-57.3 %)	93.8 % (89-98 %)	0.064	0.0-75.2
Deep position of SN with GSV	3	138	35.5 % (0.0-78.2 %)	97.2 % (95-99 %)	0.103	0.0-89.7

SN = saphenous nerve; GSV = great saphenous vein; CI = confidence intervals; τ^2 = tau-squared.

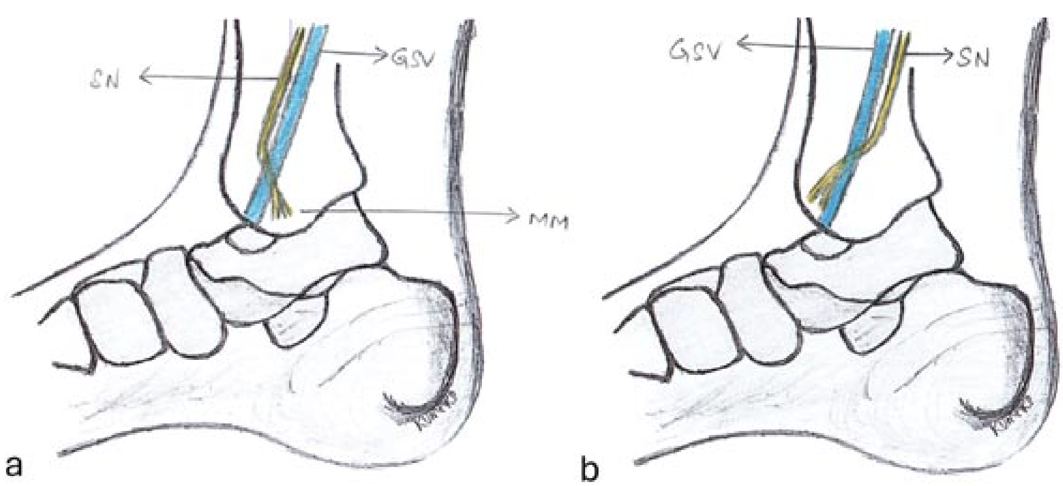

Fig.4a. Schema showing the saphenous nerve crossing the great saphenous vein from anterior to posterior aspect. Fig.4b. Schema showing the saphenous nerve crossing the great saphenous vein from posterior to anterior aspect. SN: saphenous nerve, GSV: great saphenous vein, MM: medial malleolus.

Variations in the distances between SN and GSV in the lower leg region. Seven studies did not report any data on the distances between SN and GSV among sides (Table III). Five studies have reported the distances between the SN and GSV but did not specify the sides (Table III). One study from USA reported the data on the distance between SN and GSV in right and left side as: 0.23 cm and 0.32 cm, respectively (Warehime *et al*, 2023). Another study reported the distance between SN and GSV in dorsiflexed and plantar flexed positions of the left ankle as follows: 0.27 cm and 0.31 cm, respectively (Tonogai *et al*., 2018). A meta-analysis of five studies assessed the mean distance between the great saphenous vein (GSV) and the saphenous nerve (SN) in the lower leg (Table IV & Fig. 5). The pooled mean distance using a random effects model with Hartung-Knapp adjustment was 0.27 cm (95 % CI: 0.19 to 0.36 cm; τ^2=0.0049), indicating a relatively consistent anatomical proximity between these two structures. However, substantial heterogeneity was observed among the studies (I^2 = 97.6 %, Q=254.3, $p < 0.0001$), suggesting significant variability in the reported distances, and attributable to methodological variance (80 %) and anatomical diversity (20 %) (Fig. 5).

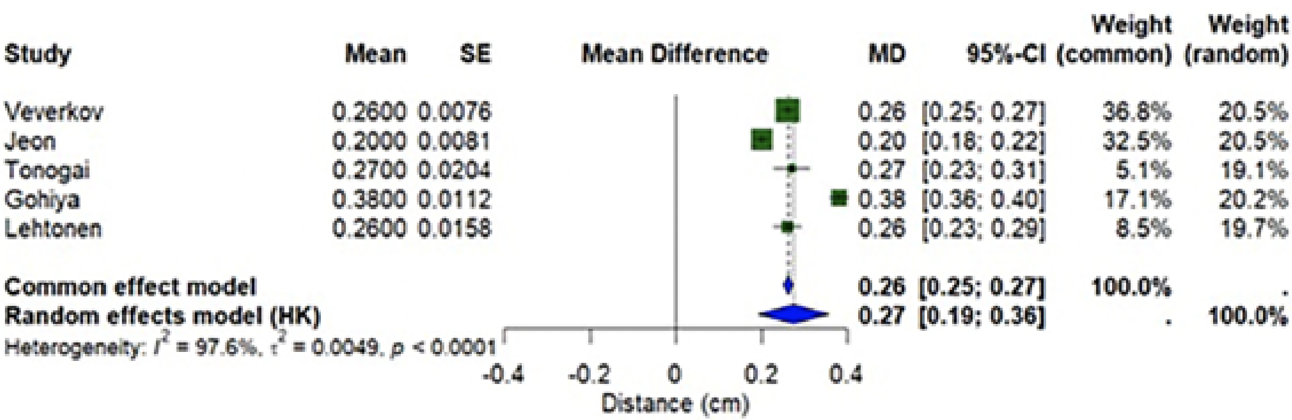

Fig. 5. Forest Plot of SN-GSV proximity using "Random-Effects" model.SE: standard error, MD: mean distance, CI: confidence intervals, HK: Hartung-Knapp, τ^2 = tau-squared.

DISCUSSION

This current study gives a comprehensive dataset on the distance of SN with GSV in the lower third of the leg. The weighted mean distance of 0.27 cm (2.7 mm) demonstrates that the SN is consistently located in dangerously close proximity with the GSV across all the populations studied. This remarkably small distance persists regardless of age, sex, or laterality, indicating that the nerve is vulnerable to iatrogenic injury during venous procedures, thermal ablation, sclerotherapy, or surgical interventions near the GSV subject to high nerve injury risk, and the lower leg region represents a particular danger zone where proximity is closest.

In addition to establishing this standard dataset on SN-GSV proximity, we also found that the positioning of SN with GSV is highly variable. These positional variations of SN and GSV in the lower third of leg should be kept in mind particularly while harvesting saphenous venous graft to avoid injury to the SN. A histo-morphological study conducted on the spatial relationship of the GSV and SN in the lower leg region revealed that the vein and artery are highly variable in their position and in most cases, they are too intimate to an extent that the adventitial layer of the GSV and the perineural sheath of the SN shared a common connective sheath (Veverkova *et al*., 2011). Such a vast positional variation of SN and GSV and structural intimacy observed in our analysis could be due to the developmental reasons, methodological differences, anatomical variation among populations, or measurement inconsistencies. Despite the heterogeneity, the direction and magnitude of the distance were consistent in all the studies included in our analysis. The development of GSV during fetal life provides valuable insights on the "angio-guiding nerves" theory. Angio-guiding nerves are known to release vascular endothelial growth factors, which further facilitate the maturation of the arterio-venous system during the 6th-8th weeks of fetal development (Uhl, 2015). Any procedural errors or the disparities in the signaling process during this critical period might contribute to the SN-GSV positional variations as observed in our study.

Since this structural intimacy and variations of GSV-SN are too obvious in the lower leg, incisions made below the knee had a higher incidence of SN injury than other approaches, especially those made at the ankle, during the ankle cutdown of GSV (Moawad *et al*., 2008). The incidence of SN paresthesia and neuralgia in the leg are higher in the conventional vein harvest (CVH) procedures compared to the minimally invasive vein harvest (MIVH) procedures. Studies reported that the incidence of SN neuralgia reduced by 3.3% with MIVH as compared to CVH which was 26.7% (Bonde *et al*., 2002; Aziz *et al*., 2006). In addition, the risk of causing damage to both GSV and SN in suture button technique performed at the tibiofibular syndesmosis was reported by Hamada *et al*. (2021). While using suture button technique, care must be taken not to affix the medial button perpendicular to the course of GSV and SN. Our data on the distance between the GSV and SN would help surgeons to work meticulously in this area to avoid or decrease the risk of impingement between the medial button, GSV and SN, respectively. A recent hospital-based study from Sri Lanka conducted on 57 patients concluded that the SN should be taken care while performing total stripping of GSV in the lower leg region to avoid complications associated with the injury of SN (Cheagar & Fernando, 2022). This study reported a wide range of complications such as numbness, tingling sensation and shooting pain at ankle region, particularly towards the medial malleolus. Such sensory deficits could be avoided by following the morphometric data we reported in our study. Our study has a few limitations. Firstly, the measurements we analyzed were limited to the lower leg region and we excluded the measurements from other regions to avoid bias in establishing the standard dataset. Secondly, we could not establish statistical differences on gender and side patterns due to inadequate data available in the literature.

In conclusion, the findings of our study indicate that the spatial relationship of the GSV and SN in the lower leg varies among individuals and differs from population to population, indicating a high-risk injury to the GSV and SN. This meta-analysis confirms that the blind approaches to the GSV in the lower leg constitute unacceptable risk. The consistently close proximity (<3 mm) combined with positional unpredictability creates a high-risk surgical environment where nerve injury is likely without precise imaging guidance. Therefore, a thorough evaluation for identifying the GSV and SN using ultrasonography techniques prior to surgical procedures in the lower leg and on the medial ankle regions will help surgeons to avoid post-surgical neuralgias particularly the SN neuralgia.

POTU, B.K.; SHIITU, B.S.; ALMARABHEH, A. y EL-DIN, W.A.N. Comprensión de la relación espacial entre el nervio safeno y la vena safena mayor en la región de la pierna: Una revisión sistemática y meta análisis. *Int. J. Morphol., 43(5)*:1537-1544, 2025.

RESUMEN: La relación anatómica entre el nervio safeno (NS) y la vena safena magna (VSM) debe tenerse en cuenta para evitar lesiones en la NS durante la extracción quirúrgica de la VSM. La relación entre el NS y la VSM es muy variable en la región de la pierna y no existe un conjunto de datos exhaustivo sobre la posición y la distancia entre el NS y la VSM en dicha región. El objetivo principal de nuestro estudio fue analizar la posición y la distancia entre la VSM y el NS en la región de la pierna. Se realizó una búsqueda sistemática de literatura utilizando las directrices PRISMA en bases de datos como MEDLINE, PubMed, SciELO y revisiones Cochrane utilizando términos de búsqueda como "nervio safeno", "vena safena magna", "distancia" y "región de la parte inferior de la pierna", que arrojó 1248 enlaces de artículos. De los catorce estudios que cumplieron con los criterios de inclusión que comprenden 592 miembros inferiores están en un rango de edad de 26-101 años. Nuestro análisis agrupado reveló que la distancia del NS con VSM en el tercio inferior de la pierna utilizando un modelo de efectos aleatorios con ajuste de Hartung-Knapp fue de 0,27 cm (IC del 95 %; $\tau 2 = 0{,}0049$), lo que indica una proximidad anatómica relativamente consistente entre estas dos estructuras. Sin embargo, se observó heterogeneidad sustancial entre los estudios ($I^2 = 97{,}6$ %, $Q = 254{,}3$, $p < 0{,}0001$), lo que sugiere una variabilidad significativa en las distancias informadas. En cuanto a la posición del NS con la VSM, la estimación combinada de nuestro estudio reveló que el NS se encuentra anterior a la VSM en el 31,4 % de los casos y posterior a ella en el 33,1 %. El predominio de NS profundos a la VSM se alinea con el 35,5 %, lo que refleja la vulnerabilidad del NS en las intervenciones quirúrgicas de la VSM. Nuestros datos proporcionan valores más representativos sobre la relación espacial del NS con la VSM en la región de la parte inferior de la pierna, y esta información sería de gran utilidad para que los cirujanos eviten lesiones del NS que pueden provocar alteraciones sensoriales en la región de la parte inferior de la pierna e incluso un neuroma del NS.

PALABRAS CLAVE: Vena safena magna; Nervio safeno; Distancia; Región de la parte inferior de la pierna; Lesión.

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