

The anatomical location of the great saphenous vein at the thigh and ankle: a neonatal cadaver study

Daniël J. van Tonder^{1,2}, Ahmad Kathrada¹, Adnan Lokhandwala¹, Martin L. van Niekerk³, Albert van Schoor²

¹Department of Anatomy and Cellular Biology, College of Medicine and Health Sciences, Khalifa University, Abu Dhabi, United Arab Emirates

²Department of Anatomy, Basic Medical Sciences Building, Prinshof Campus, Faculty of Health Sciences, University of Pretoria, South Africa

³Department of Paediatric Surgery, Faculty of Health Sciences, University of Pretoria, South Africa

SUMMARY

Providing critically ill neonatal patients with parenteral nutrition, medication, fluids, and access to blood sampling is essential in intensive care units. One option for blood sampling is the great saphenous vein within the proximal thigh, and near the medial malleolus in neonates via 'conventional' landmark and ultrasound techniques. Practitioners in many countries still use the traditional landmark approach to locate the great saphenous vein in neonates, regardless of access to ultrasound. We aim to provide measurements that accurately describe the anatomy of the great saphenous vein in neonates to aid in cannulation success.

The great saphenous vein was exposed in the proximal thigh and near the medial malleolus by reflecting the skin in 31 and 30 formalin-fixed neonate cadavers, respectively. Pins were placed at essential bony landmarks and soft tissue structures. The termination of the great saphenous

vein within the proximal thigh can be located 6.8 ± 1.5 mm inferior to the inguinal ligament. The average shortest distance from the medial malleolus to the great saphenous vein was 4.3 mm, 2.0 mm anterior, and 3.1 mm superiorly. The diameter of the great saphenous vein in the proximal thigh and at the medial malleolus ranged between 1.4 mm and 1.6 mm, and 0.9 mm and 1.1 mm, respectively with a 95% confidence level. Our results provide a more accurate description to gain venous access through the great saphenous vein. However, if available, ultrasound should be used to locate and confirm the diameter of the great saphenous vein in the lower limb.

Key words: Parenteral nutrition – Cannulation – Formalin-fixed – Ultrasound – Vascular access – Catheterization

Corresponding author:

Daniël J. van Tonder. Department of Anatomy and Cellular Biology, College of Medicine and Health Sciences, Khalifa University, PO Box 127788, Abu Dhabi, United Arab Emirates. Phone: +971 2 312 4721. E-mail: daniel.tonder@ku.ac.ae - ORCID: 0000-0001-8246-915X

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INTRODUCTION

Obtaining peripheral venous access can be difficult, but is essential in critically ill neonatal populations. Acquiring venous access in neonatal patients will allow for parenteral nutrition, medication, fluids administration, and will also provide access for blood sampling (Detaille et al., 2010; Rocha et al., 2017). Successfully cannulating venous structures on the first attempt within neonates is vital, as multiple attempts to penetrate the venous structure could result in associated pain with atypical sensitivity and behavioral changes (Ponnusamy et al., 2014). Most peripheral veins in neonates are especially small in diameter, which complicates visualization and cannulation (Ponnusamy et al., 2014). Historically, venous access was obtained using only anatomical landmarks. With the introduction of ultrasound guidance, venous cannulation is now much safer, particularly in neonates. A high-frequency linear array transducer can be used to give the best resolution without the need for significant tissue penetration (Brass et al., 2015; Bruzoni et al., 2013; Sigaut et al., 2009). However, ultrasound-guided venous cannulation is not advantageous when users have limited ultrasound training (Bair et al., 2008): this is especially true if the user does not have a good understanding of the anatomy visualized on the screen.

The great saphenous vein “*Vena saphena magna*” is the longest vein in the human body, originating at the medial foot and receiving deep pedal tributaries from the dorsal venous arch of the foot “*arcus venosus dorsalis pedis*” and the dorsal digital veins of the big toe “*venae digitalis dorsalis pedis primae*” as it courses to the medial malleolus (Caggiati et al., 2002; Kachlik et al., 2011). The great saphenous vein courses anteriorly to the medial malleolus as it moves superiorly over the postero-medial aspect of the knee joint before continuing to the saphenous opening overlying the femoral triangle, on the anterior aspect of the proximal thigh, where it terminates at the saphenofemoral junction and drains into the common femoral vein (Kachlik et al., 2011; Standring, 2020). The great saphenous vein is a suitable and safe alternative for venous access, particularly in small infants (Aria et al., 2014). Gaining vascular access through the great saphenous vein within the prox-

imal thigh can be attempted with an open surgical technique inferior to the inguinal crease and medial to the femoral artery, or through a cutaneous landmark approach (Chokshi et al., 2010). The great saphenous vein near the medial malleolus is a commonly used venous access point in neonates due to its sufficient diameter and its position to the skin (Ponnusamy et al., 2014). In addition, the great saphenous vein near the medial malleolus provides sufficient stabilization while aiding in easy cannulation into the inferior vena cava (Uygun, 2016).

Cannulation of the great saphenous vein in neonates is rarely investigated in medical literature due to its concealed nature and poor direct visibility under high-frequency ultrasounds (Bian et al., 2021). Nonetheless, it is important to note that while a limited number of studies have used the great saphenous vein as a route for central venous access in neonates and infants, there are multiple locations to puncture the great saphenous vein, including: near the medial malleolus (Bian et al., 2021), medial to the popliteal fossa (Tu et al., 2021), and within the proximal thigh below the femoral pulse (Pramod et al., 2022). Access through the great saphenous vein coincides with the logical progression of attempting peripheral venous access first, and moving to more central venous structures, minimizing complications such as thrombosis, arterial injury, or complete occlusion to central veins (Aria et al., 2014). The recommended choice for the site of peripherally inserted central catheters to minimize catheter-related blood stream infection is the great saphenous vein in relation to the medial malleolus (Sarmiento Diniz et al., 2022). This would optimize the first attempt success rate, reducing the duration of the procedure and limiting the complications of stress and pain in neonates (D’Andrea et al., 2022). In instances where the great saphenous vein is occluded, the risks associated with gaining venous access decrease (Aria et al., 2014). Furthermore, the diameter of the great saphenous vein is an important variable with respect to the success rate of cannulation. Hanada et al. (2017) and Schnadower et al. (2007) reported that the diameter of the vein has an association with the success rate of the first puncture. As such, there

is a need to provide accurate anatomical measurements of the great saphenous vein within the proximal thigh and near the medial malleolus in neonates for successful localization and venous cannulation.

This study aims to provide the location of the great saphenous vein in relation to the inguinal ligament within the proximal thigh, and to determine the shortest distance between the most prominent point of the medial malleolus and the great saphenous vein at the ankle. Moreover, we determine the diameter of the great saphenous vein in the proximal thigh and near the medial malleolus. Furthermore, we identify the necessary locations and compare literature for making incisions to guide successful location and venous cannulation in neonatal patients.

MATERIALS AND METHODS

Materials

A sample of 31 and 30 formalin-fixed neonate cadavers was used in this study to investigate the great saphenous vein near the proximal thigh and at the medial malleolus, respectively. All cadavers had been donated to the Department of Anatomy, University of Pretoria under the rules and regula-

tions of the South African National Health Act, 61 of 2003 for research and teaching purposes. Ethical clearance to conduct this study was obtained from the University of Pretoria's Faculty of Health Sciences Research Ethics Committee (ethics clearance number: 447/2018). At the time of death, all the cadavers were younger than six weeks. Cadavers were obtained and stored according to the standards set out in the South African National Health Act (61 of 2003), as well as the 1964 Declaration of Helsinki. All sample demographics are presented in Table 1 and 2. We excluded cadavers with any developmental abnormalities in the lower limb region or where previous dissections had disrupted the normal anatomy of the region.

A Vernier mechanical dial caliper (accuracy of 0.01mm) manufactured by Beta (Beta©, 2023, Beta Utensili S.P.A., Sovico, Italy) was used to make all the measurements.

Methods

Within the proximal thigh, two lateral incisions were made: one at the trans-tubercular line – the imaginary line connecting the two iliac tubercles (located on the iliac crests) – and the second approximately at the mid-thigh, from the medial surface extending anteriorly across to the lateral

Table 1. Demographic information concerning the neonatal cadavers used to measure the great saphenous vein near the proximal thigh. (n = number of individuals).

	n	Range	Minimum	Maximum	Mean	Std. Deviation
Age (days)	31	16	0	16	1.10	3.13
Height (m)	31	0.24	0.29	0.53	0.38	0.06
Weight (kg)	31	2.00	0.60	2.60	1.25	0.58
BMI	31	10.47	5.00	15.47	8.34	2.95
Male	17	-	-	-	-	-
Female	14	-	-	-	-	-

Table 2. Demographic information concerning the neonatal cadavers used to measure the great saphenous vein at the medial malleolus. (n = number of individuals).

	n	Range	Minimum	Maximum	Mean	Std. Deviation
Age (days)	30	27	0	27	2.53	5.67
Height (m)	30	0.27	0.29	0.56	0.38	0.06
Weight (kg)	30	2.40	0.60	3.00	1.27	0.64
BMI	30	10.47	5.00	15.47	8.52	2.83
Male	17	-	-	-	-	-
Female	13	-	-	-	-	-

surface. Another midline incision was made extending from the trans-tubercular line to the incision made at the thigh. The skin of the proximal thigh and the inguinal region was then reflected laterally to expose the underlying subcutaneous fat and fascia. The subcutaneous fat together with the saphenous fascia surrounding the great saphenous vein and the fascia lata superficial to the common femoral vein (Caggiati, 1999) were carefully separated to clearly see the course of the vessels. The sartorius muscle and the inguinal ligament were cleaned, so that the medial border of the sartorius and the inferior border of the inguinal ligament were clearly visible (Fig. 1a). The neonatal cadaver was then positioned and clamped supine with the thigh rotated externally. This was to simulate as much as possible the surgical position that a neonate would be placed in

when attempting to insert a catheter into the great saphenous vein in the proximal thigh. Pins were then placed on the anterior superior iliac spines, pubic tubercle, and other soft tissue structures such as the saphenofemoral junction and great saphenous vein.

The distance between the anterior superior iliac spine and the pubic tubercle was used to determine the inguinal ligament length. The midpoint termination of the great saphenous vein into the common femoral vein was projected superiorly perpendicularly to the inguinal ligament and was used to determine where the great saphenous vein terminates in relation to the inguinal ligament. The distance from the translocated point on the inguinal ligament to the termination of the great saphenous vein was measured.

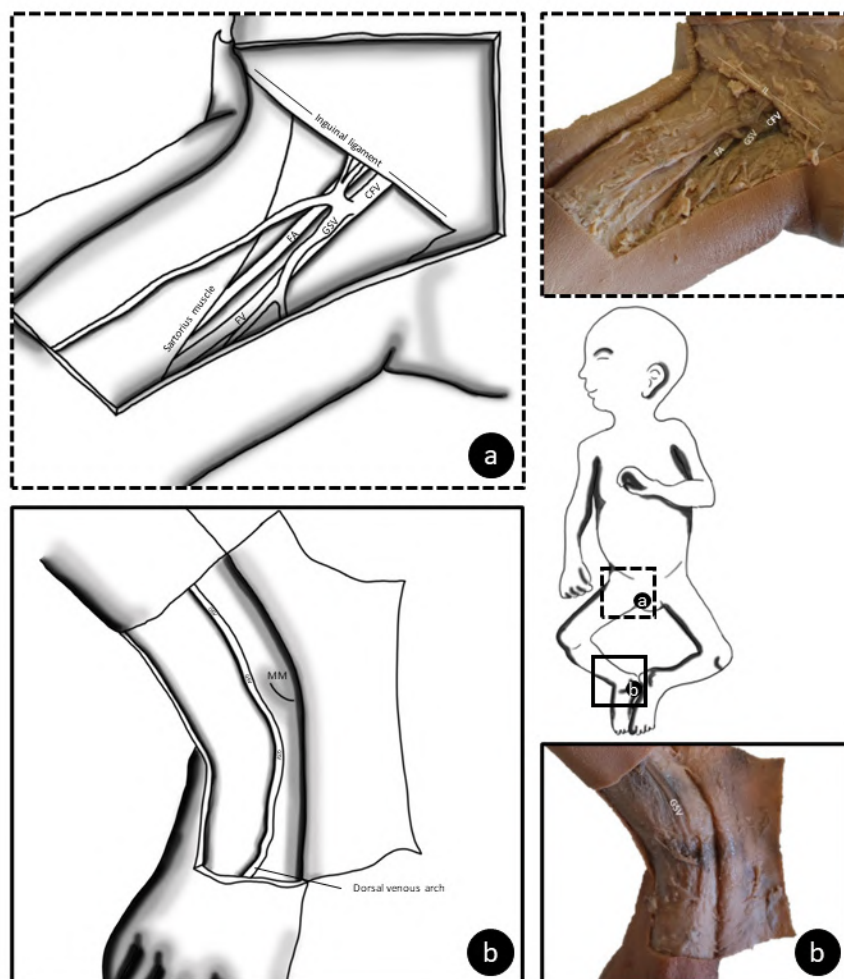


Fig. 1.- Schematic representation of the great saphenous vein within the proximal thigh and near the medial malleolus. **a)** Anterior view of the proximal thigh illustrating cleaned superficial and deep vascular structures. **b)** Medial aspect of the ankle, illustrating the course of the great saphenous vein as it courses from the dorsal venous arch of the foot superiorly. (CFV = Common femoral vein; FA = Femoral artery; FV = Femoral vein; GSV = Great saphenous vein; MM = Medial malleolus).

To expose the great saphenous vein near the medial malleolus, the skin covering the medial malleolus was reflected by making three skin incisions. The first, superior to the medial malleolus, extended horizontally from the anterior aspect of the ankle to the superior aspect of the medial malleolus. The second was inferior to the medial malleolus, extending from the anterior surface of the dorsum of the foot to the inferior aspect of the medial malleolus. Finally, the third incision was made, connecting both the anterior incisions from the anterior aspect of the ankle to the dorsum of the foot (Fig. 1b). The most prominent point on the anterior margin of the medial malleolus was identified and pinned, as well as the great saphenous vein closest to the medial malleolus. Care was taken not to disturb the course of the great saphenous vein while the vein was being exposed.

To determine the location of the great saphenous vein near the medial malleolus at the distal end of the lower limb, the measurement between the most prominent point on the anterior margin of the medial malleolus and the great saphenous vein was measured. In addition, two planes were established: the first parallel to the plantar surface of the foot – the horizontal plane – and the second perpendicular to the plantar surface of the foot – the vertical plane. The distances between the most prominent aspect of the medial malleolus and the great saphenous vein in the horizontal planes, as well as the distance in the vertical plane, will allow the location of the great saphenous vein to be described in quantitative values.

In addition, the outer diameter of the great saphenous vein within the proximal thigh and near

the medial malleolus was measured as close to the point of interest as possible. Care was taken not to compress the vein when the diameter was measured.

Statistical analysis

Statistical analysis was conducted on IBM SPSS Statistics version 27.0.1.0 (2023©, IBM®, SPSS Inc, New York USA) and summarized using descriptive statistics, including mean, median, standard deviation and 95% confidence intervals. We compared measurements from the left and right sides using a paired t-test or Wilcoxon Signed Rank test, depending on the distribution of the data determined by a Shapiro-Wilk test for normality, and after outliers were removed via standardized values. We used an inter- and intra-observer error analysis to test for repeatability and accuracy, following Bland and Altman (2010) on 25% of the sample.

RESULTS

Quantitative data

After both left and right distribution were determined to be normal with a Shapiro-Wilk test for normality, the paired t-test revealed no significant difference (p -value > 0.05) between the left and right measurements. This was followed by combining the left and right sides and producing a descriptive statistical analysis together with a 95% confidence interval.

The descriptive statistical analysis of the great saphenous vein within the proximal thigh is outlined in Table 3. The average length of the inguinal ligament in the sample was 25.5 ± 3.4 mm (mean

Table 3. Descriptive statistical analysis and 95% confidence interval in mm, after combining applicable left and right sides of the great saphenous vein in the proximal thigh. (n= number of individuals; Min= Minimum; Max= Maximum; SD= Standard deviation; GSV = great saphenous vein; IL = Inguinal ligament; PT = Pubic tubercle).

	n	Range	Minimum	Maximum	Mean		SD	95% Confidence interval for mean	
					Statistic	Std. Error		Lower	Upper
IL length	58*	14.10	19.45	33.55	25.51	0.45	3.40	24.41	26.45
GSV-IL	60	5.91	0.89	6.80	3.90	0.19	1.50	3.38	4.24
IL-PT	59*	11.71	3.09	14.80	8.17	0.33	2.50	7.57	8.97
GSV diameter	49*	1.58	0.71	2.29	1.49	0.05	0.36	1.38	1.60

*Removal of outliers reduced number of individuals

Table 4. Descriptive statistical analysis and 95% confidence interval in mm, after combining applicable left and right sides of the great saphenous vein near the medial malleolus. (n= number of individuals; SD= Standard deviation; MM = medial malleolus; GSV = great saphenous vein).

	n	Range	Minimum	Maximum	Mean		SD	95% Confidence interval for mean	
					Statistic	Std. Error		Lower	Upper
MM-GSV	55*	5.40	1.58	6.98	4.25	0.18	1.33	3.85	4.58
Horizontal plane	56*	5.03	0.05	5.08	2.03	0.14	1.05	1.69	2.23
Vertical plane	57*	5.42	0.39	5.81	3.12	0.19	1.42	2.74	3.52
GSV diameter	55*	1.24	0.49	1.73	1.04	0.04	0.29	0.94	1.10

*Removal of outliers reduced number of individuals

± standard deviation), while the distance from the termination of the great saphenous vein to the inguinal ligament averaged 3.9 ± 1.5 mm. The average distance from the termination of the great saphenous vein's perpendicular projected point on the inguinal ligament to the pubic tubercle had a mean distance of 8.2 ± 2.5 mm. The great saphenous vein's diameter ranged between 1.4 mm and 1.6 mm, with a confidence level of 95%.

The descriptive statistical analysis of the great saphenous vein near the medial malleolus is outlined in Table 4. The average shortest distance between the medial malleolus and the great saphenous vein was 4.3 ± 1.3 mm. In the horizontal plane, the average distance to the great saphenous vein from the medial malleolus was 2.0 ± 1.1 mm anteriorly. While in the vertical plane, the mean distance to the great saphenous vein was 3.1 ± 1.4 mm superiorly. With a confidence level of 95%, the average diameter of the vein ranged between 0.9 mm and 1.1 mm.

Interobserver and intra-observer error analysis

No clinically significant difference and bias for the interobserver and intra-observer measurements could be identified when Bland and Altman (2010) method was used. The results of this study were therefore considered to be repeatable and accurate.

DISCUSSION

Peripheral intravenous cannulation in neonates can present with symptoms such as extravasation, phlebitis, leakage, spontaneous dislodgment, and catheter-associated blood stream infections (Gar-

land et al., 1992; Unbeck et al., 2015). As a result, ultrasound-guided venipuncture in all ages is more attractive as it provides 'real-time' imagery, while cannulation of venous structures is attempted. The ultrasound-guided technique for cannulation of the great saphenous vein has been shown to reduce the number of attempts needed when compared to the anatomical approaches (Joshi et al., 2010). More specifically with reference to neonates, ultrasound-guided techniques have been demonstrated in terms of success rates, comfort, improved localization, and decreased total procedural times (Bian et al., 2021; Pramod et al., 2022; Tu et al., 2021). However, it has been also indicated that ultrasound-guided cannulation techniques have limited capabilities in terms of safety and quality, especially with those practitioners that have limited ultrasound training (Bair et al., 2008; Brass et al., 2015; Otani et al., 2018). Ultrasound effectiveness is significantly dependent on the training, skill, and experience of the health professional, as indicated by Schoenfeld *et al.* (2011). Further evidence shows that it takes as many as nine attempts after training to achieve a 70% probability of success in pediatric patients (Anderson et al., 2021). As such, other than the ultrasound-guided methods, the landmark approach is still commonly used for the localization of the great saphenous vein in neonates (Pramod et al., 2022; Tu et al., 2021).

Chokshi et al. (2010) state that the saphenofemoral junction is a reliable and easy route to gain central venous access. Access is achieved by making a small incision inferior to the inguinal crease and medial to the femoral artery, and the vein will be found within the subcutaneous tissue (Chokshi

et al., 2010). Dronen and Lanter (1999) located the proximal great saphenous vein in adults by making an incision 50 mm inferior to the junction between the middle and medial one-third of the imaginary line running from the pubic tubercle to the anterior superior iliac spine. In this neonatal cadaver sample, the great saphenous vein and its termination as the saphenofemoral junction was found 6.8 ± 1.5 mm inferior to the inguinal ligament. The termination of the great saphenous vein at the saphenofemoral junction perpendicularly projected to the inguinal ligament was on average 8.2 mm inferior to the inguinal ligament. The distance between the pubic tubercle and the anterior superior iliac spine, or the inguinal ligament length, was 25.5 ± 3.4 mm. The ratio between the distance from the pubic tubercle to the projected point, the great saphenous vein's ter-

mination perpendicular to the inguinal ligament and the inguinal ligament's length in this neonatal sample is one-third the distance (Fig. 2a). The diameter of the proximal great saphenous vein ranged between 1.4 mm and 1.6 mm with a confidence interval of 95%.

The great saphenous vein originates from the dorsal venous arch of the foot and courses superiorly anterior to the medial malleolus, and then runs just behind the medial aspect of the knee and is often visible on the posteromedial aspect of the knee where it curves round the top of the tibia (Kachlik et al., 2010; Lockhart et al., 2019). The site near the popliteal fossa is a good site for central venous catheter insertion. Tu et al. (2021) reported the vein diameter near the popliteal fossa of neonates to be 0.8 mm and 0.7 mm in the

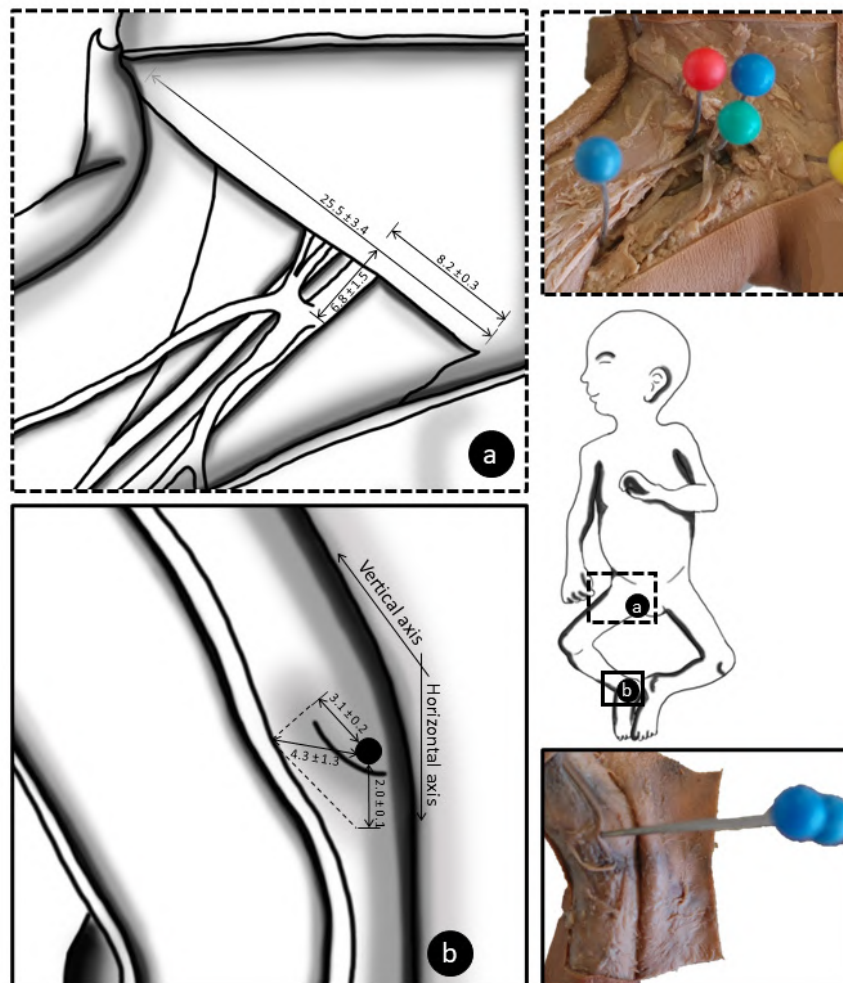


Fig. 2.- Schematic representation of the location of the great saphenous vein within the proximal thigh and near the medial malleolus. **a)** Anterior view of the proximal thigh indicating the length of the inguinal ligament the distance from the great saphenous vein to the inguinal ligament. **b)** Medial aspect of the ankle, showing the shortest distance from the most prominent point of the medial malleolus to the great saphenous vein and the distances in a vertical and horizontal axis.

ultrasound group and control group, respectively. Another variable measured in this study is termed the venous depth, which refers to the distance between the skin and the near edge of the vein.

Bian et al. (2021) conducted a randomized clinical trial, in which they explored the great saphenous vein's anatomy at the medial malleolus in 144 infants between the ages of four and nine months with congenital heart disease, using both ultrasound and conventional anatomical landmark techniques. They reported the diameter and depth of the great saphenous vein measured via both techniques were not significantly different. The depth was 3.62 ± 1.41 mm and 3.61 ± 1.42 mm for ultrasound-assisted group and 'traditional' anatomical landmark group, respectively. Additionally, the diameter of the great saphenous vein was found to be 1.49 ± 0.32 mm and 1.54 ± 0.40 mm for the ultrasound-assisted group and the 'traditional' anatomical landmark group, respectively. In addition, Triffterer et al. (2012) investigated the measurements of the great saphenous vein at the level of the medial malleolus via ultrasound-guided technique in 65 infants (less than six months of age) and neonates for venous cannulation. They reported the median diameter of neonates and infants' right lower limb's great saphenous vein as 1.5 mm (1.1 mm to 2.99 mm). Additionally, the median depth of the great saphenous vein at the site of the right leg's medial malleolus to be 4.4 mm (1.5 mm to 9.5 mm). In this study, the measured diameter of the great saphenous vein near the medial malleolus ranged between 0.9 mm and 1.1 mm, with a confidence level of 95%. Table 5 compares the different findings from the studies conducted by Bian et al. (2021),

Tu et al. (2021) and Triffterer et al. (2012). Furthermore, Triffterer et al. (2012) indicated that agenesis may be explored in the case of the great saphenous vein not being visible under high resolution ultrasound. When gaining venous access at the great saphenous vein near the medial malleolus, Puntis (1987) used a silastic feeding line with an external diameter of 0.6 mm. The silastic feeding line used by Puntis (1987) would have been appropriate for this sample population. Church and Jarboe (2017) suggest using imaging technology like ultrasound and fluoroscopy to accurately determine the diameter of the vein before venous access is gained – this would greatly increase the safety and ease of the procedure.

Triffterer et al. (2012) inferred that there is a high degree of variability of the great saphenous vein's anatomy in neonates. Wald et al. (2019) suggested finding the great saphenous vein at the medial malleolus in infants and children by using one-half to one finger width in the anterior quadrant. Chokshi et al. (2010) found that the ideal location to expose the great saphenous vein is through a small transverse incision superior and anterior to the medial malleolus. This study found the great saphenous vein superior to the medial malleolus 4.3 ± 1.3 mm in the superior anterior quadrant, and, unlike Wald et al. (2019), this would translate to a quarter of a finger's breadth. Using numeric values to determine the location will be more advantageous, as there is no standard measurement for a "finger's breadth". In this neonatal sample, the great saphenous vein can be found approximately 2.0 mm anterior and 3.1 mm superior to the most palpable part of the medial malleolus (Fig. 2b).

Table 5. Anatomical characteristics of the great saphenous vein by latest studies (2021-2022).

Study	Tu et al. (2021)	Bian et al. (2021)	Triffterer et al. (2021)	Current study
Samples	Neonates	Infants	Infants	Neonates
Vein depth (ultrasound) (mm)	2.0(0.2)	3.6(1.4)	4.4(1.5-9.5)	-
Vein depth (landmark) (mm)	2.0(0.2)	3.6(1.4)	-	-
Vein diameter (ultrasound) (mm)	0.8(0.1)	1.4(0.3)	1.5(1.1-2.99)	-
Vein diameter (landmark) (mm)	0.7(0.1)	1.5(0.3)	-	1.04(0.04)
Location of GSV measurement	Popliteal fossa	Medial malleolus	Medial malleolus	Medial malleolus

Note: Measurements unless stated are represented means (standard deviation). Triffterer et al. (2021) reported their measurements in Median (range).

There were no “strong” correlations seen when comparing any measurement of the great saphenous vein within the proximal thigh or near the medial malleolus with the weight, height, or BMI of the sample.

In conclusion, the great saphenous vein within the proximal thigh can be located 6.8 ± 1.5 mm inferior to the inguinal ligament, and medial to the pulse of the femoral artery, and the diameter of the vein will range between 1.4 mm and 1.6 mm, with a confidence interval of 95%. The great saphenous vein near the medial malleolus in this sample can be located by making an incision 4.3 ± 1.3 mm anterosuperior to the medial malleolus in the anterosuperior quadrant. This implies that the great saphenous vein could be located if an incision was made 2.0 mm anterior and 3.1 mm superior to the most prominent palpable part of the medial malleolus. A silastic feeding tube with an external diameter of 0.6 mm could be ideally cannulated into the great saphenous vein at the medial malleolus. These anatomical guidelines provide a more accurate description in the pursuit of gaining venous access in the great saphenous vein at two anatomical locations. However, if available, and using the anatomical information that was presented in this study, ultrasound guidance should be used in order to locate the great saphenous vein prior to attempting venous access.

Limitations

This study has several limitations. As with any dissection of formalin-embalmed cadavers, we encountered tissue stiffness. In addition, tissue shrinkage could be present within the embalmed neonatal cadavers. Measuring the diameter of the great saphenous vein on a living population of neonates using ultrasound should be considered a more accurate measurement. Although we took great care not to disrupt the vein when measuring the diameter of the great saphenous vein, the fact that it was done on a cadaveric sample should be taken into account.

DECLARATIONS

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved (Ethics clearance number:

447/2018) by the Health Sciences Research Ethics Committee at the University of Pretoria, South Africa. All methods and observations were carried out in accordance with the relevant requirements, guidelines, and regulations stipulated in the South African National Health Act (61 of 2003), as well as the 1964 Declaration of Helsinki.

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The authors sincerely thank those who donated their bodies to science so that anatomical research could be performed. Results from such research can potentially increase mankind’s overall knowledge that can then improve patient care. Therefore, these donors and their families deserve our highest gratitude.

Authors’ contributions

DJ van Tonder: Protocol development, Data collection, Data analysis, Manuscript writing, Literature research, Critical review

A Kathrada: Manuscript writing, Literature research, Critical review

A Lokhandwala: Manuscript writing, Literature research, Critical review

ML van Niekerk: Protocol development, Manuscript editing, Critical review

A van Schoor: Protocol development, Data collection, Data analysis, Manuscript writing, Literature research, Critical review

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