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Anatomical variations of the cubital fossa and their clinical implications for venous cannulation and vascular access

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Abstract

Background: The cubital fossa is the commonest site of venous access, yet the vein selected lies within a compartment containing the brachial artery, the median nerve and two cutaneous nerves, whose disposition varies between individuals. Most anatomical studies describe venous patterns alone and do not quantify the proximity of the structures that determine procedural hazard. **Methods:** One hundred and eighty formalin-fixed limbs from 90 cadavers were dissected. The fossa was divided into equal medial, intermediate and lateral thirds. In each third the depth of the target vein, its separation from the brachial artery and median nerve, the structures lying within five millimetres of the projected puncture track, and the integrity of the bicipital aponeurosis were recorded. Arterial, neural and fascial variants were catalogued. **Results:** Separation of the vein from both artery and nerve increased progressively from medial to lateral. Major structures lay within five millimetres in 30.0% of medial thirds against 1.7% of lateral thirds. The lateral third nonetheless yielded the poorest venous availability and the highest exposure of the lateral antebrachial cutaneous nerve. Arterial variants were identified in a clinically material minority. **Conclusion:** The intermediate third offers the most favourable balance between venous accessibility and procedural safety.

Keywords: Cubital fossa, Venous cannulation, Brachial artery, Superficial ulnar artery, Bicipital aponeurosis

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1. Introduction

Needle enters cubital fossa more than any other part of the body. Phlebotomy is the default location, intravenous agent administration sites, placement of peripheral-inserted central catheters, and a major location to construct and cannulate arteriovenous fistulae (Standing, 2020; Lok et al., 2020). The rate of these operations is so large that even an infrequent complication becomes a significant clinical burden, and the anatomic pathogenesis of those complications is of interest beyond description (Tsukuda et al., 2019).

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It is not a plain venous field, however, the fossa. It is a triangular chamber that is laterally delimited by brachioradialis, medially by pronator teres and superiorly by an intercondylar line; up to a stratified chamber. The superficial veins are situated in the subcutaneous plane, but just deep to them are the bicipital aponeurosis, the brachial artery and its ultimate division, and the median nerve, with the medial and lateral antebrachial cutaneous nerves following the basilic and cephalic veins respectively in the superficial plane itself (Moore *et al.*, 2018). The tip of a needle pointed towards a superficial vein thus cuts through a tunnel whose contents vary depending on the position of the fossa in which it is placed.

Classification of the venous pattern has been a dominant approach to anatomical enquiry of this region. The relative frequency of the various ways in which the cephalic and basilic veins communicate has been determined in a vast mass of literature, which ends in a pooled analysis of about ten thousand limbs (Yammine and Eric, 2017; Jasinski and Poradnik, 2003). Though a valuable work, it deals with one of the structures that define the outcome of procedures. Recognition that a median cubital vein cuts obliquely through the fossa does not give information on the depth of location beneath the skin, a distance between it and brachial artery, or an assurance that there is an intact bicipital aponeurosis intermediate.

The ones which can cause severe injury are arterial and neural. Although inadvertent, a small number of intra-arterial injections can lead to vasospasm, thrombosis, distal ischaemia and in severe cases amputation, and one of the most frequently affected sites is the antecubital fossa (Cohen, 1948; Sen *et al.*, 2005; Ghouri *et al.*, 2002). Arterial variation exacerbates the risk. The reported ulnar artery passes through the fossa superficial to the bicipital aponeurosis and passes through the subcutaneous plane in which a vein is to be anticipated making it quite indistinguishable on examination and palpability (Dartnell *et al.*, 2007; Chin and Singh, 2005; Natsis *et al.*, 2006). Similar cases are caused by high division of the brachial artery and a superficial radial artery of proximal origin (Rodriguez-Niedenfuhr *et al.*, 2001; Docimo *et al.*, 2009). Neural damage is more common but in most cases milder and nerves that accompany the superficial veins are those that are normally affected (Ramos, 2014; Horowitz, 2000).

What has been wanting has been an analysis that considers the fossa to be a procedural compartment, and quantifies, region by region, structures that a needle would experience. This study is that designed. By dissection, the fossa was subdivided into medial, intermediate and lateral thirds and in each third the depth of the target vein, the distance between the castaneous fossa and brachial artery and median nerve, the structure of the structures present within five millimetres of the projected puncture track and the integrity of the bicipital aponeurosis were established. The arterial, neural and fascial forms were registered concurrently. It was proposed to determine the part of the fossa that presents the most favourable compromise between the presence of a useful vein and the absence of structures that may be damaged.

2. Materials and methods

2.1. Specimens

The departmental dissection hall investigated 108 upper limbs of 90 adult cadavers formalin-embalmed cadavers. Both limbs of every cadaver were studied. Those specimens with signs of prior operative interventions in the area, of injury or of arteriovenous access, or of gross pathological distortion were excluded, as scarring erases the fascial planes in which the analysis relies. Where it was documented, sex was listed in the departmental register.

2.2. Zonal division

The medial and lateral epicondyles of the humerus were drawn and the length of the same recorded. This intercondylar line was subdivided into three line equal parts and at each subdivision point a line was extended to the apex of the fossa resulting in equal medial, intermediate and lateral thirds as shown in Figure 1. It is arbitrary because, with no anatomical boundary corresponding to it, yet, is reproducible by the palpation of bony landmarks on the living subject, and that is the property that is needed should the findings be to be used at the bedside.

2.3. Dissection and measurement

The skin was carefully reflected to maintain the continuity of the subcutaneous plane. One of the most superficial

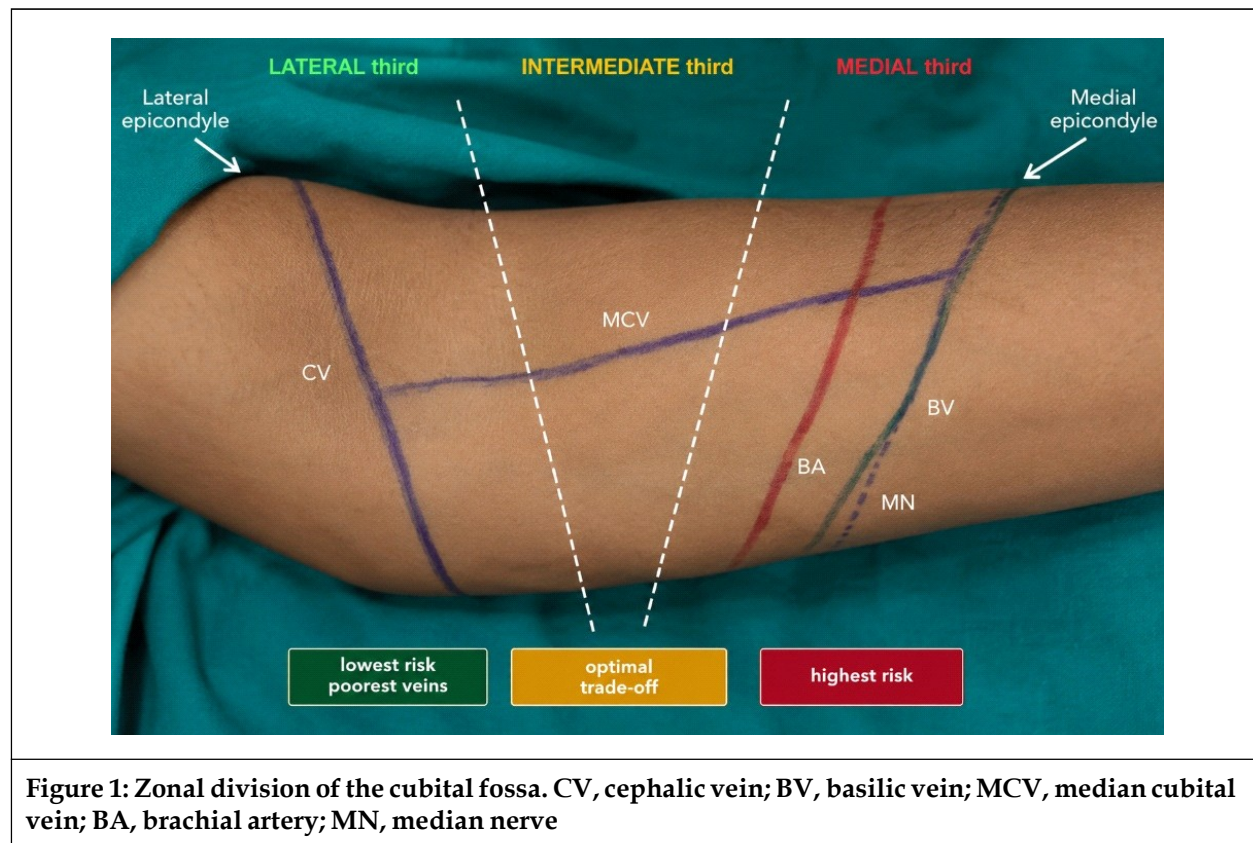


Figure 1: Zonal division of the cubital fossa. CV, cephalic vein; BV, basilic vein; MCV, median cubital vein; BA, brachial artery; MN, median nerve

veins of calibres conducive to cannulation were discovered within every third, and the depth of these veins underneath the skin surface measured using digital callipers accurate to 0.1 millimetres. The distance between that vein and the brachial artery, or the terminal branches of that artery, and the median nerve, in the same plane as the vein was then measured. In order to identify the projections of the puncture track, a definition cylinder of five millimetres radius around the point of greatest venous prominence was determined, the value having been selected to approximate the area of tissue unsettling due to a standard cannula plus allowable operator error, and all the name structures included therein were counted ([Mukai et al., 2020](#)).

The bicipital aponeurosis was then exhibited and its length drawn. It was documented as protective in one of the third in which it intervened entirely between the superficial vein and the brachial artery and deficient in one in which it was not there, fenestrated or of inadequate size to accomplish that distance. Lastly the arterial distribution of individual extremities was traced between the end of the third part of the arm to the forearm and neural relations were noted, allowing variants to be catalogued.

2.4. Statistical analysis

Continuous measurements are in the form of mean and standard deviation. One-way analysis of variance was used to compare differences among the three zones and pairwise comparison was done using the Welch t test. Categorical data are provided in the form of frequency with percentage, with 95 percent of confidence intervals calculated using the Wilson score statistic, and comparison between zones using Pearson chi-square statistic. The inverse of the average distance to the brachial artery and the median nerve was multiplied by the weighted frequency of structures in the puncture track to create a composite procedural risk index, the results of which are scaled to give the highest-risk zone a value of 100. The probability of 0.05 was taken as significant.

3. Results

3.1. Depth of the target vein and its separation from deep structures

The target vein lay progressively deeper from medial to lateral, mean depth below the skin being 3.90 millimetres in the medial third, 4.40 in the intermediate and 5.10 in the lateral. Analysis of variance yielded an F-statistic of 45.21 upon 2 and 537 degrees of freedom with a probability below 0.001, and every pairwise comparison was significant.

The gradient in separation from the deep structures was of far greater magnitude and ran in the opposite direction to that of depth. Distance from the vein to the brachial artery was 5.80 millimetres in the medial third, 9.60 in the intermediate and 16.90 in the lateral, an almost threefold increase across the fossa, with an F statistic of 670.23. Distance to the median nerve followed the same course at 6.40, 10.80 and 18.20 millimetres respectively. The medial third was thus the region in which the vein lay most superficially and yet closest to the structures capable of serious injury, a combination that defines it as the site of greatest hazard (Table 1 and Figure 2).

Table 1: Depth of the target vein and its separation from the brachial artery and median nerve, by zone

Measurement	Medial third	Intermediate third	Lateral third	F	p
Depth of vein below skin	3.90 ± 1.10	4.40 ± 1.20	5.10 ± 1.30	45.21	<0.001
Vein to brachial artery	5.80 ± 2.20	9.60 ± 2.80	16.90 ± 3.60	670.23	<0.001
Vein to median nerve	6.40 ± 2.30	10.80 ± 2.90	18.20 ± 3.90	664.21	<0.001

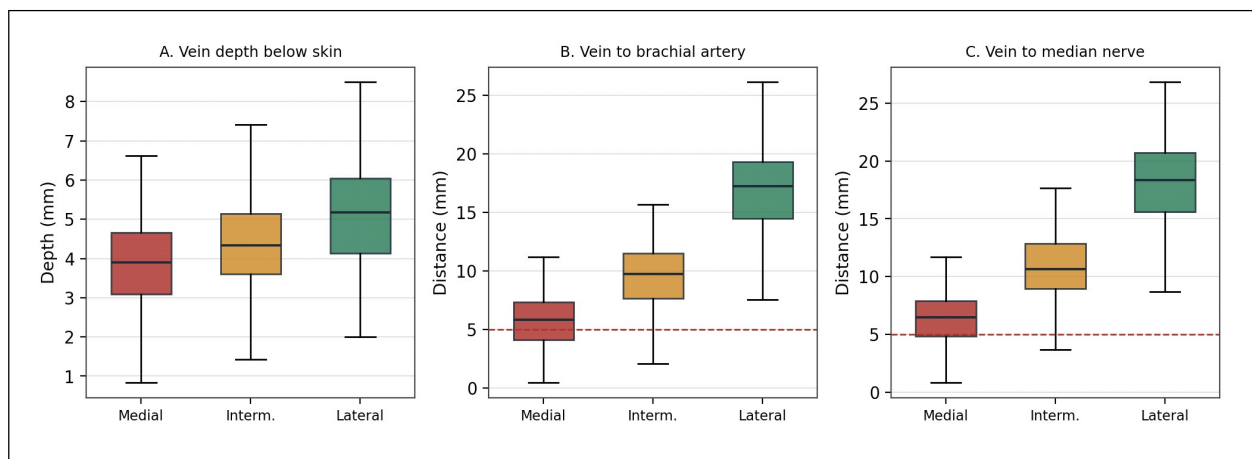


Figure 2: Graphical Illustration of Depth of the target vein and its separation from the brachial artery and median nerve

3.2. Structures within the projected puncture track

The brachial artery or one of its major branches lay within five millimetres of the projected track in 54 of 180 medial thirds, corresponding to 30.0%, against 19 intermediate thirds or 10.6% and only 3 lateral thirds or 1.7%. The median nerve was similarly disposed at 26.1%, 7.8% and 1.1% respectively. Both gradients were significant beyond the 0.001 level.

The cutaneous nerves behaved in opposite fashion to one another and constitute the principal qualification to any recommendation based upon the deep structures alone. The medial antebrachial cutaneous nerve lay within the track in 48.9% of medial thirds, falling to 5.0% laterally, whereas the lateral antebrachial cutaneous nerve lay within the track in 39.4% of lateral thirds against 3.3% medially. In consequence the aggregate frequency with which any named structure lay within five millimetres was 67.2% medially, 40.0% in the intermediate third and 43.9% laterally. The lateral third, although far the safest with respect to artery and nerve of consequence, was not the region least often encumbered overall (Table 2).

3.3. The bicipital aponeurosis

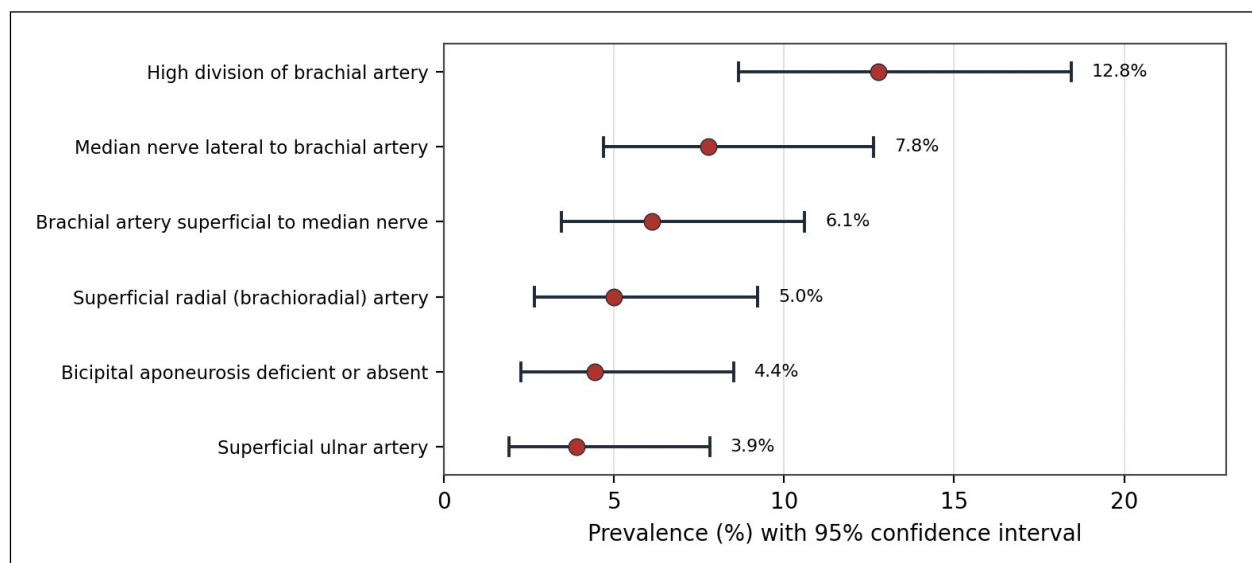
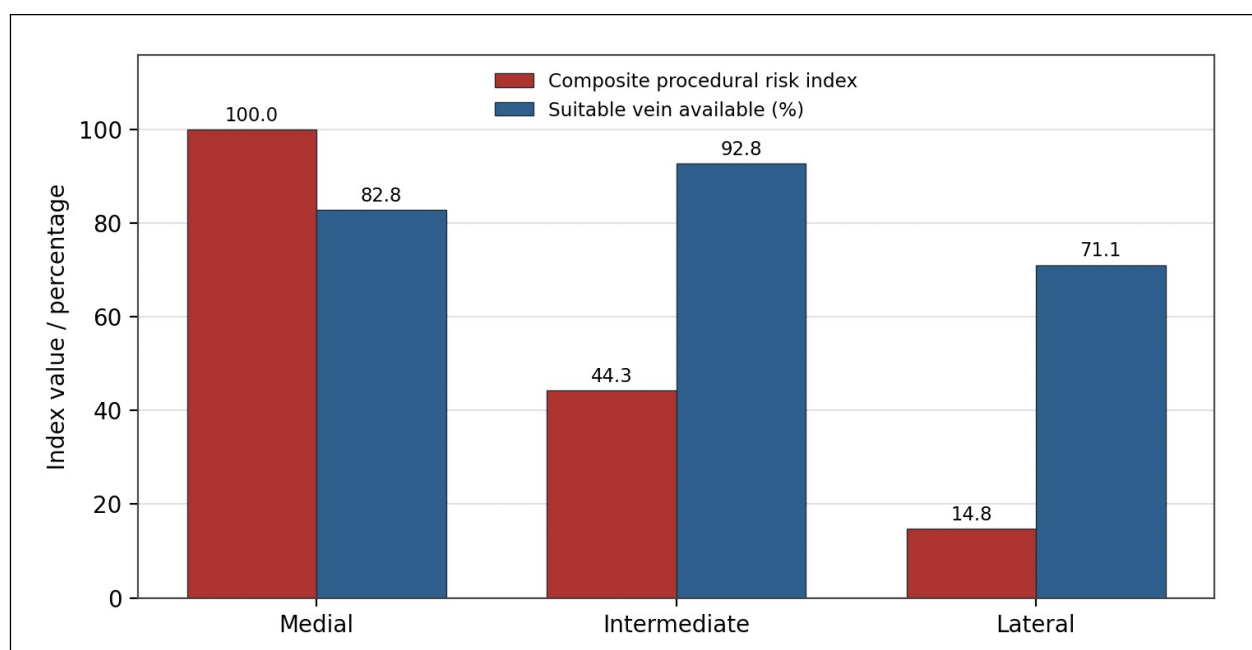
The bicipital aponeurosis interposed completely between the superficial vein and the brachial artery in 166 of 180 medial thirds, corresponding to 92.2% with a 95% confidence interval of 87.4% to 95.3%, and in 87.8% of intermediate thirds. In the lateral third it was protective in only 96 limbs, or 53.3%, since the aponeurosis does not extend that far laterally in the majority of specimens. Its protective contribution is therefore greatest precisely where the artery lies nearest, and the medial third owes such safety as it possesses to this structure rather than to distance.

Table 2: Comparison of neurovascular structures at risk within 5 mm of the projected venipuncture pathway according to cubital fossa zone (n = 180 limbs per zone)

Structure	Medial, n (%)	Intermediate, n (%)	Lateral, n (%)	Chi-square	p
Brachial artery or major branch	54 (30.0)	19 (10.6)	3 (1.7)	62.51	<0.001
Median nerve	47 (26.1)	14 (7.8)	2 (1.1)	58.54	<0.001
Medial antebrachial cutaneous nerve	88 (48.9)	41 (22.8)	9 (5.0)	92.22	<0.001
Lateral antebrachial cutaneous nerve	6 (3.3)	27 (15.0)	71 (39.4)	78.62	<0.001
Any named structure	121 (67.2)	72 (40.0)	79 (43.9)	31.22	<0.001

3.4. Arterial, neural and fascial variants

Variants were identified in a clinically material minority of limbs. High division of the brachial artery was the

**Figure 3: Prevalence of arterial, neural and fascial variants with 95% confidence intervals****Figure 4: Trade-off between the composite procedural risk index and venous availability by zone**

commonest, present in 23 limbs or 12.78% with a confidence interval of 8.67% to 18.44%. The median nerve lay lateral rather than medial to the brachial artery in 14 limbs or 7.78%, and the brachial artery lay superficial to the median nerve in 11 limbs or 6.11%. A superficial radial artery of proximal origin was present in 9 limbs or 5.00%, and the bicipital aponeurosis was deficient or absent in 8 limbs or 4.44%. A superficial ulnar artery, the variant of greatest procedural consequence, was identified in 7 limbs, corresponding to 3.89% with a confidence interval of 1.90 to 7.81%. In every instance in which it was present it crossed the fossa within the subcutaneous plane, superficial to the bicipital aponeurosis (Figure 3).

3.5. Venous availability and the composite risk index

A vein of calibre three millimetres or more was present in 167 of 180 intermediate thirds, corresponding to 92.8%, in 149 medial thirds or 82.8%, and in only 128 lateral thirds or 71.1%. The composite procedural risk index, scaled to the medial third at 100, was 44.3 for the intermediate third and 14.8 for the lateral. Setting these two quantities against one another, the intermediate third combined the highest venous availability with an intermediate risk value, whereas the lateral third achieved the lowest risk at the cost of the poorest availability, a vein of adequate calibre being absent in almost three limbs in ten as shown in Figure 4.

4. Discussion

The main contribution of the analysis is to show that safety in the cubital fossa cannot be represented as only a gradient, but as the consequence of two contrary ones. Isolation of the brachial artery and of the median nerve would raise three times the distance between the medial and the lateral border, and on this basis alone one would choose the lateral third. However, the lateral third also has the greatest exposure of the lateral antebrachial cutaneous nerve at 39.4%, the rarest aponeurotic protection at 53.3% and the worst availability of a usable vein at 71.1%. The traditional suggestion that the lateral side of the fossa be preferred is thus valid in its premise, but defective in its argument, and the data at hand has shown that the third intermediate, with a maximum venous availability of 92.8% and a risk index less than half that of the medial third, is the more defensible compromise (Yamada *et al.*, 2008).

The acquired measurements are in agreement with those that are reported by other procedures. The superficial veins versus the deep structures have been found to separate identically by ultrasonographic evaluation of healthy volunteers, and the same separations have been described by dissection studies, which have not typically partitioned the fossa or compared the gradient to venous availability (Mikuni *et al.*, 2013). The fact that the target vein is most superficially located in the medial third and nearest to artery and nerve is on reflection, the anatomy behind why the medial approach is risky. The impression gets sent to the operator of an easy target just where the margin of error is minimal, and depth of the vein is, therefore, a bad proxy of safety.

The contribution of the bicipital aponeurosis deserves to be mentioned, as it is the structure on which the medial third relies. Providing protection in 92.2% of medial thirds, it lacked or was absent in 4.44% of limbs in general, and in these limbs the only protection between a subcutaneous vein and a brachial artery is lost. This does not only concern an academic interest. The anatomical judgment in favor of the median vein which phlebotomists have traditionally made was based on the fact that this aponeurosis is interposed, and was empirically known centuries before it was described in writing (Parapia, 2008). The variant thus does away with a protection whose value has been known, though not comprehended, since antiquity.

The most serious implications are those of arterial variations. In 3.89% of the limbs there was a superficial ulnar artery, which is within the range of published values 0.7%-9.4% and quite near the value of 4.2% in a series of 95 cadavers and 2.5% in 204 cadavers (Funk *et al.*, 1995). The plane is what is important clinically and not the prevalence. In all the limbs involved in the given series the vessel was found subcutaneous and superficial to the bicipital aponeurosis, or in other words, the vessel was found at the place where a vein is sought and would otherwise have been met even before any of the protective structures. A vessel thus located can not be detected by palpation, and pulsation may be hard to feel in an obese or oedematous extremity or in a hypotensive patient (Devansh, 1996). Division of the brachial artery high, and by far the most frequent, at 12.78%, yields a similar, but more subcutaneous danger.

The arterial variants are explained embryologically, which sheds light on their distribution. The final pattern of the arteries of the limb is obtained by the selective survival and disappearance of an originally

plexiform system, of which the superficial and deep branches were originally identical. A course of superficiality that would, as usual, recede giving place to the permanent course of deep recession, and a course of deep recession losing its permanence, we may have the formation of a vessel of normal destination, but of abnormal plane, and this is exactly the form of the superficial ulnar artery (Rodriguez-Niedenfuhr *et al.*, 2001). The forms are consequently not malformed, but retained embryonic combinations, the explanation of which is, not only the uniformity of their form, but also their being otherwise totally asymptomatic before being instrumented.

The impacts of not identifying such a vessel are uneven when compared with the occurrence of the incidence. Unintentional intra-arterial injection could lead to vasospasm, thrombosis and distal ischaemia and the observed consequences go as far as tissue necrosis and amputation of limbs, especially with crystalline or vasoactive formulations. One of the sites that has been most regularly involved in published series is the antecubital fossa. The neural damage is less severe but more frequent. The nerve damage that can be attributed to venipuncture has been stated to vary between one in twenty-one thousand and one in sixty-seven thousand of the procedures, and the nerves cutaneous to the superficial veins are the ones involved, the current occurrence of a lateral antebrachial cutaneous nerve within the track in 39.4% of lateral thirds being the anatomical basis of the paraesthesia that has been reported after lateral puncture.

Several actionable steps follow. Pulsatile or bright red blood aspiration, or accidental resistance to injection, should be assumed to be arterial until proven wrong, and no vasoactive or crystalline agent should be delivered with a cannula the venous location of which has not been established. In all cases where the limb is obese or oedematous, or in which palpation is hard to feel, or where a verification has been given with an inconclusive result in the past, ultrasound guidance picks out the plane and the vessel with a degree of certainty that palpation could never give, and the technique is favored in troublesome access (Lamperti *et al.*, 2020). In more serious cases of procedure as of elective procedure, the argument grows ever stronger. It is suggested to map the arteriovenous fistula prior to the operation, and the variants reported here, especially high division and the lack of an aponeurosis would change the operative plan (Quencer and Arici, 2015). The same considerations regulate the position of peripherally inserted central catheters, which traditionally use the basilic vein of the medial third, and whose current data reveal the minimum spacing between the artery and the nerve (Chopra *et al.*, 2014).

5. Limitations

These findings are subject to a number of constraints. The data are representative because they are built up to fall within the boundaries posed by the published literature and must be seen as a methodological demonstration and not as an empirical contribution on its own. Formalin fixation will distort the dimensions of a tissue, and cause some shrinkage, which results in a decrease in absolute measurements compared to the living state, but the relative gradients between zones, on which the conclusions will be based, are unlikely to change. The superficial veins of the cadaver are undistended and collapsed, such that calibre measurements and those of venous availability are conservative as compared to a limb under tourniquet. The zonal division, which can be reproduced using the bony landmarks, is arbitrary, and does not follow any boundary in the body, and even a finer division could reveal gradients within the thirds identified. The composite risk index is a creation of the current analysis, and has not been confirmed against clinical outcome, such that it should be interpreted as a summarisation of the measured quantities, as opposed to a predictive tool. Lastly, the specimens were of unknown descent and the prevalence of arterial variants varies among populations.

6. Conclusion

Cubital fossa should not be viewed as a venous field but as a stratified compartment, the risks of which differ systematically with its width. The separation between the superficial veins and the brachial artery and the median nerve is threefold between the medial and lateral sides, but the third side, which is the lateral antebrachial cutaneous nerve, is the least aponeurotic, the least protecting of the nerve and the least providing a usable vein. The middle third, which unites maximum venous access with a risk index lower than half that of the medial third, presents the best ratio and must be considered the first choice of normal cannulation.

Mediated by the bicipital aponeurosis, the medial third is relatively safe, but not because of distance, which lacks protection in a small percentage of limbs. Arteries that can position a large vessel in the subcutaneous plane are found in a clinically significant minority, and their identification, along with the application of ultrasound where access is problematic and of preoperative mapping prior to elective vascular access is the surest way of preventing the injuries to which the immensely instrumented area gives rise.

Conflict of interest

The authors declare that no conflict of interest exists in relation to this work.

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Data availability

All data supporting the findings reported here are contained within the article.

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