

## Bleeding varicose veins' ulcer as a cause of death: a case report and review of the current literature

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### Abstract

Chronic venous insufficiency (CVI) and varicose veins (VVs) of the lower limbs are very frequent vascular diseases in Western countries. One possible complication of these conditions is skin ulceration and its consequent rupture, which can be spontaneous or due to mild or trivial trauma. In some cases, the resulting hemorrhage is fatal. When the victim is found dead, a large amount of blood around the body might lead to the hypothesis of violent death. The Forensic Pathologist needs to be very careful in the corpse's examination, in order to exclude any alternative cause of death. Herein, an illustrative case is reported, as well as a literature review of the literature concerning sudden hemorrhages from VVs. We found 27 scientific papers, the total reported cases of VVs rupture with profuse hemorrhages were 36, 32 of which were fatal. The main characteristics of such forensic scenario have been collected. Corpse examination of the victims showed pallor of the skin and mucous membranes, as well as marked pallor of organs as a sign of hemorrhagic shock, but these pathological findings are unspecific. Usually, the skin near the ulcer presented color alteration (discoloration and atrophy or pigmentation and hyperemia). Besides, the histological examination of the skin could be a valid instrument to demonstrate the presence of the ulcer, even if it could be very difficult to sample, because of its small size. An important limit of our study is the small number of collected cases. More studies in this field are needed to improve evidence concerning death due to VVs rupture. *Clin Ter 2021; 172 (5):e395-406. doi: 10.7417/CT.2021.2346*

**Key words:** Varicose veins, ulcerations, fatal hemorrhage

### Introduction

Chronic venous insufficiency (CVI) and related varicose veins (VVs) of the lower limbs are some of the most common vascular diseases of Western countries (1-4). The pathogenesis of VVs and CVI is related to valve reflux and incompetence (5). It has been suggested that cytokines released in chronic inflammation processes could also contribute to the vein wall and valve alteration (6). The most common

complications related to CVI and VVs are leg edema, eczema of the skin surrounding VVs, ulceration, and spontaneous rupture (7). Usually, the latter has no fatal consequences, even if some cases of death have been reported (8). In such cases, a large amount of blood around the victim might lead to the hypothesis of violent death, whereas the real cause of death usually is hemorrhagic shock due to the spontaneous bleeding from the ulcer. Herein, we present the case of a woman found dead in her home in a pool of blood with no apparent traumatic lesions. A careful body examination revealed VVs with a point-like solution of continuity of the skin. A systematic review of the literature concerning deaths caused by profuse hemorrhage from the rupture of a VV of the lower limb is also performed, in order to collect the present knowledge about the prevalence and main characteristics of this forensic scenario. The aim of this work is to identify the pathological findings that can help the Forensic Pathologist to make the correct diagnosis of death in such suspicious cases.

### Methods

The present systematic review was carried out according to the Preferred Reporting Items for Systematic Review (PRISMA) standards. A systematic literature search and a critical review of the collected studies were conducted. An electronic search of PubMed, Science Direct Scopus, Google Scholar, and Excerpta Medica Database (EMBASE) from database inception to March 2021 was performed. The search terms were "varicose veins", "rupture", "hemorrhage", "death", "bleeding", and "autopsy" in the title, abstract, and keywords. The bibliographies of all located papers were examined and cross-referenced to further identify relevant literature. A methodological appraisal of each study was conducted according to the PRISMA standards, including an evaluation of bias. The data collection process included study selection and data extraction. Two researchers (AM and AC) independently examined the papers with titles or abstracts that appeared to be relevant and selected those that concerned rupture and bleeding from a varicose vein of the

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lower limbs. Disagreements concerning eligibility among the researchers were resolved by consensus. Preprint articles were excluded, only papers in English were included. Data extraction was performed by three investigators (AB, CB, and ACM) and verified by other investigators (AM, MDP and ET). This study was exempt from institutional review board approval, as it did not involve human subjects.

## Results

A review of the titles and abstracts as well as a manual search of the reference lists were carried out. The reference lists of all identified articles were reviewed to find missed literature. This search identified 232 articles, which were then screened to exclude duplicates. The resulting 197 reference lists were screened based on their abstract, which left 89 articles for further consideration. In addition, non-English papers were excluded, and the following inclusion criteria were used: (1) original research articles, (2) reviews and mini-reviews, and (3) case reports/series. These publications were carefully evaluated, taking into account the main aims of the review. This evaluation left 27 scientific papers comprising original research articles, case reports, and case

series. Figure 1 illustrates our search strategy.

Simpson (9) and MacVie (10) were the first authors to report several cases of fatal and nonfatal bleeding from varicose veins, in 1865 and 1901 respectively. We decided to not include these articles in our review because they were too old and it was not possible to extract any precise scientific information. After these first case reports, we found other 36 cases in literature from 1912 to the present. Table 1 illustrates the results of our research and a summary of the main information about the cases.

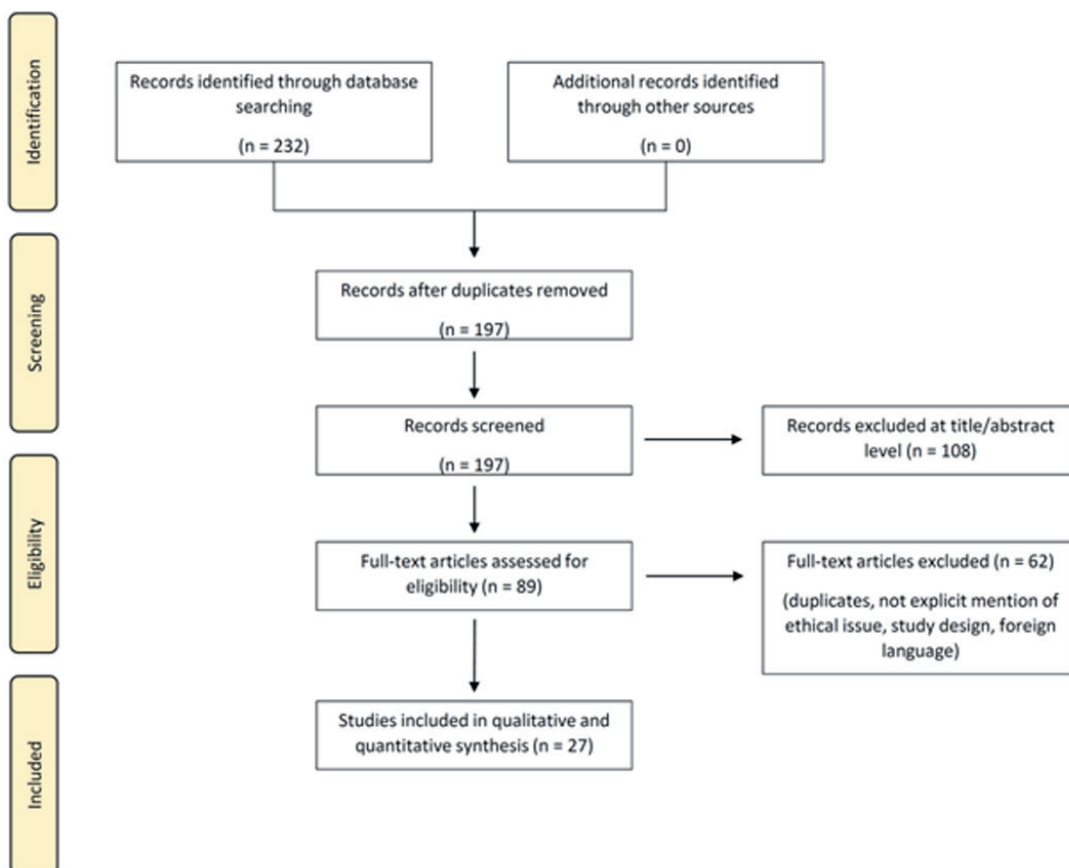


Fig. 1. An appraisal based on titles and abstracts as well as a hand search of reference lists was carried out. The resulting 232 references were screened to exclude duplicates, which left 197 articles for further consideration. The following inclusion criteria were used: (1) original research articles, (2) reviews and mini-reviews, (3) case report/series, and (4) English papers. These publications were carefully evaluated taking into account the main aims of the review. This evaluation left 27 scientific papers.

Table 1. Published case reports on massive hemorrhage from VVs. CVI indicates chronic venous insufficiency; DM, diabetes mellitus; HT, hypertension; ICAs, internal carotid arteries; LAD, left anterior descending artery; LV, left ventricle; NIDDM, non-insulin-dependent diabetes mellitus; VV, varicose veins. The symbol Ø indicates diameter. \* Two cases are presented in the paper, but one is in common with Sauvageau et al. 2007.

Reference	N. of cases	Sex and age (y.o.)	Where the subject was found	Previous medical conditions	Death (yes/no)	N. of ulcers	Characteristics of the ulcer (location, dimension)	Involved vessel	Characteristics of the skin near the ulcer	Histopathological characteristics of the ulcer	Specific autopsy findings
Macht 1912	1	F, 50	Home	Not specified	yes	1 (traumatic)	The middle of the right calf. Ø = 3 mm	Small saphenous vein or vena saphena parva's branch	Not specified	Walls of the VV: calcification and sclerotic changes	Pallor of intestines and liver
Evans et al. 1973	4	F, 54	Bedroom	VVs	yes	2	Medial right ankle. Ø = 2 mm; the other, 3 cm proximal the previous ulcer. Ø = 2 mm	Posterior arch vein	Normal skin near the ulcer	Not specified	Pallor of internal organs
		F, 83	Bedroom	Not specified	yes	1	Back of the left calf. Ø = 4 mm	Not specified	Varicose eczema	Blood-clot at the base of the ulcer	Pallor of internal organs
		F, 51	Bedroom	VVs	yes	1	Anteromedial aspect of the left lower leg. Ø = 2 cm	Not specified	Not specified	Base infiltrated by hemosiderin-laden macrophages and lymphocytes, fibrosis and calcification	Not specified
		M, 41	Taken to the hospital	VVs	No	1	6 cm above the left ankle. Ø = 5 mm	A posterior arch vein's tributary vein	Cutaneous pigmentation	-	-
du Toit et al. 1985	1	F, 57	Admitted to the hospital	VVs, HT	No	1	Left lateral malleolus. Ø = 15 mm	Saphenofemoral vein, ankle perforators	Cutaneous pigmentation	-	-
Wigle and Anderson 1988	1	F, 48	Home	History of alcohol abuse, mild HT	yes	1	Right lateral supramalleolar area. Ø < 5 mm	Not specified	Not specified	Not specified	Not specified
Morrow et al. 1994	3	M, 75	Home	Not specified	yes	1	Medial aspect of the left ankle. Ø = 5 mm	Not specified	Atrophic and discolored purplish brown. Brawny edema at the ankles	Thrombotic material and scattered acute and chronic inflammation at the ruptured margin; protein-rich exudate at ulcer surface containing scattered acute and chronic inflammatory cells	Not specified
		F, 69	Bathroom	Anticoagulant therapy (not confirmed)	yes	1	Left ankle. Ø = 5 mm	Not specified	Atrophic and shiny with multiple pigmented areas and reddish-purple scars. Edema of the ankles	Epidermis attenuated, necrotic wall of the vessel underlying the epithelium, replaced by eosinophilic layered fibrin. Dilated capillaries in the dermis, chronic inflammatory cells and macrophages containing light brown pigment	Not specified
		F, 75	Kitchen	Not specified	yes	1	Just inferior to the right medial malleolus. Ø = 5 mm	Not specified	Atrophic skin	Fibrin and granulation tissue at the edges of the ulcer; acute hemorrhage, fibrin and microvesicles in the epidermis	Not specified

## FOLLOWS

Racette and Sauvageau 2005	1 *	M, 61	Home	Not specified	yes	1	Left leg. $\varnothing = 1$ cm	Not specified	Blue blebby lesions	Not specified	Not specified
Komai et al. 2006	1	M, 56	Emergency unit of the hospital	VVs	No	1	Left calf. $\varnothing = 10$ cm	Arteriovenous communications	Skin pigmentation	-	-
Byard et al. 2007	2	F, 60 F, 86	Bedroom Home	Not specified Not specified	yes yes	1 1	Anterior to the right lateral malleolus. $\varnothing = 2$ mm Lateral aspect of the right lower calf. $\varnothing = 3$ mm	Saphenous vein Not specified	Varicose eczema Not specified	Not specified Not specified	Not specified Not specified
Sauvageau et al. 2007	1	M, 84	Bathroom	Superficial VVs for which he had been awaiting surgical intervention	yes	1	Internal surface of the left foot arch. $\varnothing = 5$ mm	Saphenous vein's tributary veins	Both legs presented hyperemia and cutaneous atrophy	Not specified	Not specified
Tollefsen 2007	1	F, 55	Home	VVs	yes	1	Right knee	Not specified	Not specified	Not specified	Not specified
Cocker and Nyamekye 2008	1	M, 85	Bath	VVs bleeding 4 weeks previously	yes	Not specified	Not specified	Right saphenofemoral junction	Not specified	Not specified	Not specified
Cittadini et al. 2008	1	M, 82	Bedroom	Not specified	yes	1	Medial surface of the left ankle. $\varnothing = 5$ mm	Not specified	Blue blebby lesions, cutaneous pigmentation with trophic changes, telangiectasia	Not specified	Pallor of internal organs
Hejna 2009	1	M, 43	Sand stack	Superficial VVs	yes	1	Internal surface of the right shank. $5 \times 3.5$ cm	Great saphenous vein	Atrophic and discolored greyish brown; right ankle with brown edema	Not specified	Not specified
Apostolidou C et al. 2010	1	F, 76	Home	Not specified	yes	2 (cat)	Inferior surface of the left leg, above the malleolus. $\varnothing = 2.5$ and $1.2$ cm	Not specified	Palm-sized skin discoloration	Not specified	Generalized ischemia of internal visceral organs
Doberentz et al. 2011	2	F, 78	Bathroom	HT, depressive syndrome, slight VVs	yes	1	Left heel. $\varnothing = 1-2$ mm	Not specified	Not specified	Not specified	Bloodless organs, shock kidneys
		M, 56	Bathroom	Not specified	yes	1	Right lower leg. $\varnothing = 1-2$ mm	Not specified	Subcutaneous skin induration	Not specified	Not specified

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Ampanozi et al. 2011	3	F, 61	Home	History of vein thrombosis for which she was taken anticoagulant	yes	1	Internal surface of the left ankle. 2 x 3.5 cm	Not specified	Not specified	Not specified	Not specified	Not specified
		F, 86	Home	-	yes	1	Left leg. Ø = 5 mm	Not specified	Not specified	Not specified	Not specified	Not specified
		M, 29	Store	Treatment with anticoagulant, not confirmed	yes	1	Internal surface of left knee. Ø = 2 mm	Not specified	Not specified	Not specified	Not specified	Not specified
Nikoli and Zivkovi 2011	1	F, 77	Porch floor	Not specified	yes	1	Internal surface of the medial aspect of the right calf	Saphenous vein	Blue blebby lesions	Not specified	Not specified	Not specified
Jelev and Alexandrov 2011	1	F, 55	Home	Not specified	yes	1	Postero-medial aspect of right upper leg. Ø = 4 mm	Greater saphenous vein's superficial tributary vein	Normal skin	Thrombotic material and acute and chronic inflammatory cells at the margin; adjacent dermis: dilated capillaries, inflammatory cells, and collagen fibers; epidermal layer: increased thickness with marked dermal papillae	Not specified	Not specified
Shimada 2012	1	F, 81	Transported to the hospital	Clopidogrel treatment; high ligation of the right saphenous vein 2 years previously	No	1	Area of anterior tibial vein	Great saphenous vein and the perforator of anterior tibial vein	Not specified	-	-	-
Fragkouli et al. 2012	1	F, 66	Home	Not specified	yes	1	Internal surface of left lower leg. Ø = 7 mm	Not specified	Not specified	Not specified	Dermis: numerous small and medium-size blood vessels, filled with blood and surrounded by thick organized fibrous cuff; fibrosis and abundant macrophages	Pallor of organs
Gilbert and Byard 2017	1	M, 84	Bathroom	HT, hypercholesterolemia, chronic back pain, VVs	yes	1	Right lower leg 25 mm above the sole. Ø = 2.5 mm	Not specified	Surrounding dermal fibrosis with hemosiderin deposition	Not specified	Not specified	Not specified
Aquila et al. 2017	1	M, 88	Bedroom	Not specified	yes	1	Left leg. Ø = 5 mm	Arteriovenous fistula (dorsal venous arch- arcuate artery)	Diffuse skin discoloration	Not specified	Not specified	Exsanguination's typical signs
Murty 2018	1	M, 54	School's bathroom	DM, HT	yes	2 (traumatic)	Right ankle. 7 x 5 x 2 mm and 6 x 4 mm	Not specified	Skin scarring and sclerosis	Scarred skin and sclerosed vessels	Not specified	Pallor of organs

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The majority (88.9%) of subjects, that presented a sudden hemorrhage from an ulcerated varicose vein, died from hemorrhagic shock due to the bleeding (3, 11-34). Out of 36 cases analyzed, 63.9% were females (3, 7-10, 12, 14, 18-21, 23, 24, 28-30, 35, 36). Most of the deceased subjects were found at their own home (3, 7-16, 18-20, 23-27, 30). Three of four cases reported by Evans *et al.* (8) had a previous medical history of varicose veins, as well as the 57 years old woman who was admitted to the hospital as described by du Toit in 1985 (31) and another consistent number of other cases reported in literature (13-15, 17, 19, 25, 29, 32, 37). In addition, Morrow and coll. (10) and Ampanozi *et al.* (20) reported an anticoagulant therapy history regarding three of their cases, even if the therapy was not confirmed in two of them. In four cases out of 36, the origin of the ulcer which led to sudden hemorrhage was traumatic (7, 18, 27, 29): one of them was caused by a cat scratch (18), another by a rooster attack (29). The remaining ulcerations were spontaneous. Regarding the lateralization of the ulcer, 61.1% of cases were located on the left leg (3, 8, 10, 11, 13, 16, 18-20, 24, 26, 28, 29, 31, 33), whereas the remaining 38.9% were on the right leg (7-10, 12, 14, 17, 19, 21, 23, 25, 27, 30). In more detail, 36.1% of the bleeding lesion were located at the level of the ankle and malleolus (3, 8, 9, 10, 12, 16, 18, 20, 27, 31), 16.7% at the level of the calf (7, 8, 12, 21, 29, 33) whereas in 25% of cases ulcers were located in other remaining parts of lower leg (3, 8, 13, 17, 19, 24, 25, 28). The majority of Authors (55.5%) did not report vessels involved in the formation of varicosity and the resulting ulcer. When reported, great and small saphenous veins with their superficial tributary vessels were the most involved (25%) (3, 7, 12, 13, 17, 21, 23, 28, 32), followed by arch veins (8, 26) and sapheno-femoral junction (15, 31). In addition, in two cases an arteriovenous fistula was held to be responsible for the bleeding (8-12, 14, 16, 18-20, 24, 25, 27, 29, 30). Characteristics of the skin near the ulcer are another interesting aspect to focus on. Only 63.9% of Authors described cutaneous alterations or normal skin near the principal lesion, whereas the remaining 36.1% did not specify if some skin changes occurred around the ulcer. The most frequent alteration was cutaneous discoloration and/or atrophy, that was reported in 22.2% of total cases (10, 13, 17, 18, 26, 28). It was followed by skin pigmentation and hyperemia (19.4%) (8, 10, 13, 16, 30, 31, 33), edema (13.9%) (3, 10, 17, 30) and skin fibrosis (11.1%) (10, 19, 25, 27). In 8.3% of cases varicose eczema and/or blue blebby lesions were described near the ulcer (3, 8, 11, 12, 16, 21), whereas in 5.5% telangiectasias were observed (16, 30). As regards to histopathologic characteristics of bleeding ulcers, in 69.5% of cases authors did not mention any specific finding. In contrast, the most frequent feature, when microscopical alterations were reported, was the presence of hemosiderin deposit in macrophages and lymphocyte infiltration (8, 10, 24, 28), but also neo-vascularization or vessel dilation in the dermis (both reported 11.1% of cases) (10, 23, 24, 28). In 8.3% of cases calcification and sclerosis of the vessel's wall was described (7, 8, 27), and the same percentage is attributable to the fibrosis and/or sclerosis of the dermis (23, 24, 27). Some Authors also found typical infiltration by cells of chronic (8.3%) and/or acute (5.5%) inflammation (10, 23). In 5.5% of cases loss of superficial

epidermis was described, whereas only in one case a fibrin deposit in epidermis was found (10). Subjects who died underwent autopsy: the cause of the death was explicitly attributed to hemorrhagic shock due to the massive bleeding for most of them (3, 7, 9-13, 15-19, 21, 24-30). The unique specific autopsy finding was the pallor of internal organs, that was reported in 30.5% of cases (7, 8, 16, 18, 19, 24, 26-28, 30). Table 2 resumes and gathers the most important information we extracted from the papers.

### Case report

A 90-year-old woman, who lived alone, was found lifeless at her home. The woman's son had been alarmed by no response at the phone and went to the mother's house, where he discovered her body slumped on the toilet bowl. There was heavy blood staining around her body as well as blood running down her left leg (see Figure n. 2).

Moreover, a heavily blood-soaked towel was tied around her left leg. The Police found some blood-soaked swabs and a bottle of antiseptic near the body, and bloody footprints in the bathroom and other rooms. The house inspections excluded obvious signs of violence. A judicial autopsy was performed to establish the cause of death and exclude the hypothesis of a crime. The external examination showed pale skin and mucous membranes, abundant blood staining of the lower limbs with a point-like solution of continuity, with telangiectasias on the nearby skin (see Figure n. 3 A), located on the mid-lateral aspect of the left leg, 34 cm above the calcaneus.

In particular, a blood stain was evident starting from this lesion and pouring down the leg (see Figure n. 2). A careful squeezing of the lesion resulted in leaking of some blood drops. There were no other traumatic lesions. The internal examination revealed pale organs. Histologic studies were undertaken on formalin-fixed tissue from all organs, showing non-specific morphological findings (hemorrhage and parenchymal necrosis) consistent with "shock organs". The left leg skin lesion was also sampled. The histological examination showed a segment with removal of the epidermis and dermis with consequent deep dermis exposure (see Figure n. 3B). Besides, deep dermis presented an altered zone with the appearance of a stratified squamous epithelium layer. In the rest of the microscopic slide, diffuse chronic atrophic skin changes were seen. The sample did not include any vessel. Toxicological screening was negative. The complete autoptic procedure and histological examination of organ tissues excluded any alternative cause of death, so eventually the death was attributed to hemorrhagic shock.

### Discussion

We described the case of a middle-aged woman who died because of the rupture of a VV on the left leg with overwhelming and fatal bleeding. VVs of the lower limbs are a diffuse Public Health concern in Western countries (1-4). The prevalence of VVs varies from < 1% to 73% in women and from 2% to 56% in men (2). VVs have consistently

Table 2 . Summary of the main characteristic extrapolated from the results of our systematic review. All frequencies (except those marked with an asterisk) have been calculated on the total of 36 cases reported. VV indicates varicose veins. \* These frequencies have been calculated on the total of dead subjects (32)

Characteristics	Frequency	References
Sex	63.9% females 36.1% males	(3) (11-14) (16) (18) (22-25) (27) (28) (32-36) (12) (14) (15) (17) (19) (20) (21) (23) (24) (29-31) (37)
Place where subjects were found	75% home 25% other places or taken to the hospital	(3) (11-20) (22-24) (27-30) (32) (34) (12) (21) (24) (25) (31) (33) (35-37)
Previous history of VV?	36.1% varicose veins 63.9% not mentioned	(12) (17-19) (21) (23) (29) (33) (35-37) (3) (11-16) (20) (22-25) (27) (28) (30-32) (34)
Previous anticoagulant therapy?	11.1% yes 88.9% not mentioned	(14) (24) (3) (11-13) (15-23) (25) (27-37)
VV rupture/ulceration etiology	11.1% traumatic 88.9% spontaneous (no trauma reported)	(11) (22) (31) (33) (12-17) (20-25) (27) (29-37)
Outcome	88.9% dead 11.1% survived	(3), (11-34) (12) (35-37)
Ulcer location	Laterality	(3) (12) (14) (15) (17) (20) (22-24) (28) (30) (32) (33) (35) (37) (11-14) (16) (18) (21) (23) (25) (27), (29) (31) (34)
	Exact location on the leg	61.1% left lower limb 38.9% right lower limb 36.1 % ankle/malleolus 22.2% lower part of the leg 16.7% calf 8.3% upper part of the leg 16.7% not mentioned

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	<p>25% saphenous vein (great and parva)</p> <p>8.3% arch veins</p> <p>5.5% sapheno-femoral junction</p> <p>11.1% other (including arteriovenous communication)</p> <p>58.3% not mentioned</p>	<p>(3) (11) (16) (17) (21) (25) (27) (32) (36)</p> <p>(12) (30)</p> <p>(19) (35)</p> <p>(30) (35-37)</p> <p>(12-16) (18) (20) (22-24) (28) (29) (31) (33) (34)</p>
<p>Involved vessel</p>	<p>22.2% discoloration and atrophy</p> <p>19.4% pigmentation/hyperemia</p> <p>13.9% edema</p> <p>11.1% skin induration/scar/fibrosis:</p> <p>8.3% eczema</p> <p>8.3% blue blebby lesions</p> <p>5.5% teleangectasias</p> <p>5.5% normal skin</p> <p>36.1% not mentioned</p>	<p>(14) (17) (21) (22) (30) (32)</p> <p>(12) (14) (17) (20) (34) (35) (37)</p> <p>(3) (14) (21) (34)</p> <p>(14) (23) (29) (31)</p> <p>(3) (12) (16)</p> <p>(15) (20) (25)</p> <p>(20) (34)</p> <p>(12) (27)</p> <p>(12) (13) (16) (18) (19) (23) (24) (28) (33) (36)</p>
<p>Characteristics of the skin near the ulcer</p>	<p>12.5% hemosiderin-laden macrophages and/or lymphocytes infiltration</p> <p>12.5% vascular alteration/neo-vascularization of dermis</p> <p>9.4% calcification/vein wall sclerosis</p> <p>9.4% chronic inflammation</p> <p>9.4% fibrosis/sclerosis of dermis</p> <p>6.3% acute inflammation</p> <p>6.3% loss of superficial epidermis</p> <p>3.1% fibrin deposit in epidermis</p>	<p>(12) (14) (28) (32)</p> <p>(14) (27) (28) (32)</p> <p>(11) (12) (31)</p> <p>(14) (27)</p> <p>(27) (28) (31)</p> <p>(14) (27)</p> <p>(14) (33)</p> <p>(14)</p>
<p>Histopathological characteristics of the ulcer*</p>	<p>34.4% reported</p> <p>65.6% not mentioned</p>	<p>(3) (12) (13) (15-25) (21) (29) (30) (34) (36-37)</p>
<p>Specific autopsy findings*</p>	<p>34.4% organs pallor</p> <p>65.6% not mentioned</p>	<p>(11) (12) (20) (22) (23) (28) (30) (31) (32) (34)</p> <p>(3) (12-19), (21) (23-25) (27) (29) (33) (35-37)</p>



Fig. 2. The woman was found lifeless in her home's bathroom. On the floor, a pool of blood. A staining of blood running down her left leg was evident.

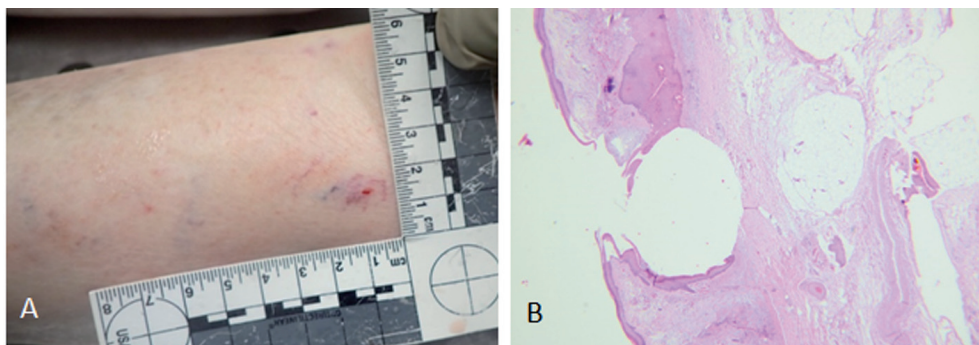


Fig. 3. A shows the point-like ulcer with telangiectasias. B shows the ulcer's histological examination (E&E).

been considered as a women's disease, even if some studies found a higher or comparable prevalence in men (1, 38). It is also believed that VVs prevalence increases with aging (39, 40). Many further risk factors have been reported, such as family history, pregnancy, and obesity, whereas there is no agreement about other potential risk factors, such as standing occupation, dietary, and smoking (2, 5, 41). The pathogenesis of VVs and CVI is related to valve reflux; Browse *et al.* argued that weakening of vein wall could cause venous dilatation and consequent valve incompetence. Another mechanism that could contribute to valve incompetence seems to be mediated by cytokines released in chronic inflammation processes (2). As in the case we presented, possible complications of CVI and VVs are ulceration and spontaneous rupture of the involved vessels and above skin (3). In the literature, at least 36 cases of sudden hemorrhage due to VVs rupture have been described (see Table n.1). Of

those, only 11.1% were traumatic and often only a mild or trivial trauma was reported. The other 88.9% were described as spontaneous. Despite the small number of cases in the literature, the real prevalence of this phenomenon could be higher since the VVs and CVI are such diffuse conditions. Maybe cases of death due to VVs rupture are under-reported because researchers underestimated their value.

The majority of cases we collected were fatal. In such cases, a huge amount of blood is usually found around or near the victim, which might lead to the hypothesis of a crime. Therefore, the Forensic Pathologist has to distinguish between a natural or a violent death, which is not always obvious. As expected, the most reported cause of death in such cases is hemorrhagic shock due to the huge loss of blood. Even if blood loss is a frequent scenario in Forensic Pathology, the diagnosis of hemorrhagic shock is not easy to prove, and often it is a diagnosis of exclusion of other causes of death

(42-45). Pallor of the skin, mucous membranes, and organs is a sign of hemorrhagic shock, alongside intestinal edema and "shock organs" appearance (42). Those signs are nonspecific and so it is very important to carefully investigate any other possible cause of death. In case of VVs rupture with ulceration of the skin, external examination of the corpse is of key importance. Whole-body skin has to be evaluated to identify any traumatic or atraumatic lesion. The VV ulcer is usually very tiny, located predominantly on the leg. We found the most described site of ulceration are the ankle and the malleoli, maybe because this body part could be easily subjected to micro-traumas that facilitate VVs rupture. It is also crucial to evaluate carefully the blood stains. For example, in the case we presented, the blood clearly poured from the skin lesion down to the leg and then to the gown. To corroborate the hypothesis of VVs ulcer, the Forensic Pathologist has also to collect an accurate anamnesis from the victim's family members or friends, when possible, and to look for leg skin alterations suggestive for CVI. The main characteristic of the skin near the ulcer described in the cases we collected is the alteration of the skin color (discoloration and atrophy in 22.2%, pigmentation and hyperemia in 19.4%). Those findings could be suggestive of CDI and VVs. The histological examination of the skin could be a valid instrument to demonstrate the presence of an ulcer. Nevertheless, it could be arduous to correctly sample the ulcer, due to its small size. Moreover, the involved vessel is not often encompassed in the sample, as in our case and the other cases described in the literature. A great limit of our study is the small number of cases collected reviewing the literature. More studies in this field are needed to improve evidence concerning death due to VVs rupture.

## Conclusions

VVs are a common condition that affects thousands of people in Western Countries. However, only a few cases of death due to the rupture of a VV with skin ulceration have been reported in the literature. Nevertheless, the real prevalence of this phenomenon may be underestimated. In such cases, diagnosis of the cause of death could be a challenge. The cause of death is usually a hemorrhagic shock due to a paramount loss of blood. But pathological signs of hemorrhagic shock are unspecific. The Forensic Pathologist has to be very careful in investigating the corpse's external appearance, alongside the internal examination. Any possible alternative cause of death needs to be excluded, before diagnosing hemorrhagic shock due to loss of blood from a VV ulcer. Histological analysis of the skin could help diagnosing the ulcer, even if it is particularly difficult to sample the involved vessel alongside the skin. Through a case presentation, we highlighted the main issues concerning the diagnosis of death in those situations, while through the systematic review of the literature we collected the main findings related to death due to VVs rupture, in order to provide a better understanding of such Forensic scenarios.

## Ethical approval

Not required.

## Author contributions

AM and AC independently examined the papers with titles or abstracts that appeared to be relevant and selected those that concerned rupture and bleeding from a varicose vein of the lower limbs. AB, CB, and ACM performed the data extraction and the case report. AM, MDP, and ET verified the results. Each author gave final approval to the version of the manuscript submitted for publication and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Conflicts of interest statement

The Authors declare that there are no conflicts of interest.

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