

On the Utility of Nailfold Capillaroscopy in Detecting the Effects of Fibrinoid Microclots in Diseases Involving Blood Stasis

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ABSTRACT: A variety of chronic, inflammatory vascular and autoimmune diseases are accompanied by fibrinoid microclots. Such diseases reflect endothelial dysfunction and may be detected using a ‘structural’ assay in the form of the fluorescence microscopic or flow ‘clotometry’ analysis of suitably stained platelet-poor plasma. Their amyloid nature and the presence of anti-fibrinolytic molecules therein make the fibrinoid microclots comparatively resistant to the normal processes of clot degradation. By inhibiting the free flow of blood, the many effects of fibrinoid microclots include those causing hypoxia, oxidative stress, and ‘blood stasis’ in the microcirculation. Nailfold capillaroscopy is an established observational technique (with both ‘structural’ and ‘functional’ elements) for assessing the microcirculation, and it is thus of interest to establish whether it too demonstrates changes when these syndromes are diagnosed. All diseases in which both methods have been applied show both the presence of fibrinoid microclots and changes in capillary properties, indicating the complementary value of the structural and functional assays. This also suggests the potential value of nailfold capillaroscopy in a variety of other diseases involving coagulopathies or a deficient microcirculation, which has been little studied to date.

Keywords: Nailfold capillaroscopy; Nailfold videocapillaroscopy; Fibrinoid microclots; Microcirculation; Inflammation; Coagulopathies; Blood stasis; Vascular and immunological disorders



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1. Introduction

More than a decade ago it was discovered, via scanning electron microscopy, that blood can clot into a highly anomalous form, which in contrast to the normal thrombi with individual fibres that appear like nicely cooked spaghetti, adopted a morphology, referred to as ‘dense matted deposits’, that instead resembled parboiled spaghetti that had congealed into an amorphous mass (e.g., [1–3]). It was subsequently recognised (e.g., [4–6]) that the ‘anomalous form’ was amyloid in nature, as it could be stained with the well-established amyloid stain thioflavin T [7–10]. Such clots were commonly in the range 2–200 µm diameter, were found in a variety of chronic, inflammatory diseases [11] (including Alzheimer’s [12–14], Parkinson’s [15,16], type 2 diabetes [12,17,18] and rheumatoid arthritis [19]) and—as all amyloids—were significantly resistant to the normal routes of fibrinolysis via plasmin(ogen) [20]. Because of their amyloid nature, we have come to refer to them as fibrinoid microclots [21–25]. Figure 1 shows a typical example of the microclots as stained with three different amyloid-selective stains.

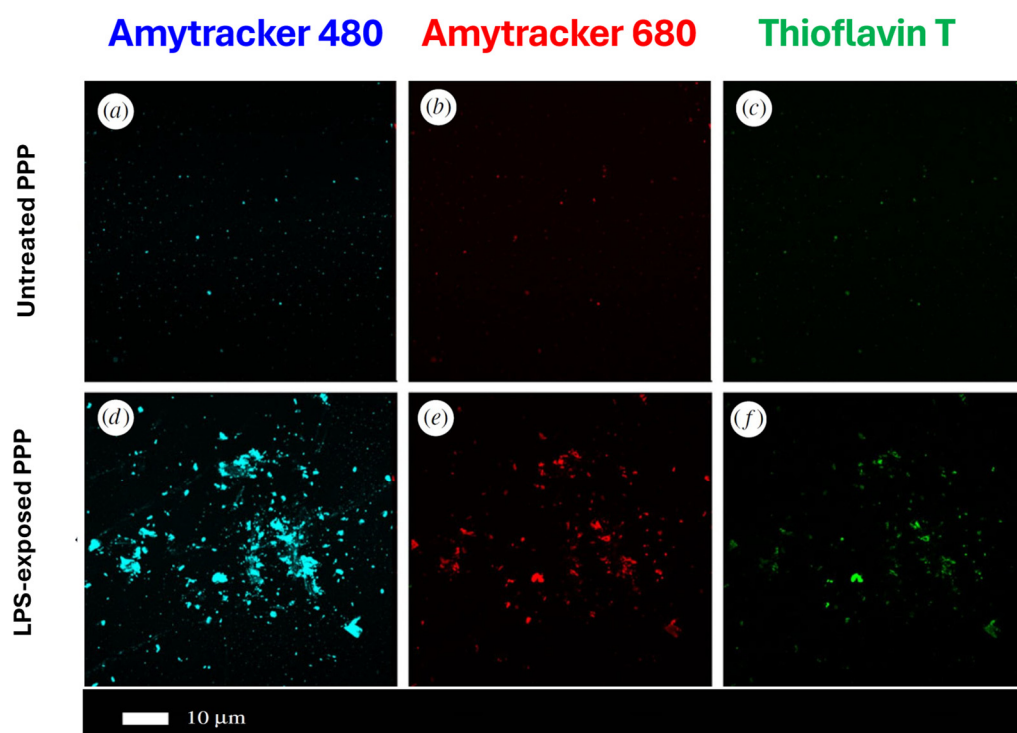


Figure 1. A typical example of fibrinolytic microclots. Platelet-poor plasma was treated with thrombin and stained either with one of two oligothiophene [26–28] Amytracker™ dyes (a,b,d,e) or with thioflavin T (c,f). In one case (d–f), a small amount of bacterial lipopolysaccharide was added prior to the thrombin. Modified from the CC-BY 4.0 publication [6].

More recently, fibrinolytic microclots have been recognised as a major feature accompanying both acute [18,29] and Long COVID [24,30–36], as well as in the related Myalgic encephalopathy/chronic fatigue syndrome (ME/CFS) [23,34,37] and sepsis [38]. As with any inert matter of this type and size (including microplastics [39–41]), fibrinolytic microclots can become trapped in microcapillaries, thereby restricting blood flow and oxygen transport to tissues. This provides ready explanations for a variety of phenomena, especially those associated with Long COVID, such as fatigue [21], post-exertional symptom exacerbation [42], postural orthostatic tachycardia syndrome (POTS) [43], and fibromyalgia [44].

Proteomic studies [30,38,45] indicate [46] a high prevalence of amyloidogenic proteins in fibrinolytic microclots that, in contrast to normal clots [47], do not reflect those in the typical normal plasma proteome [46], and this has predictive power [48,49]. In addition, both the microclots [50–52] and the thrombectomised macroclots observed [53,54] following an ischaemic stroke are amyloid in nature. Amyloidogenic cross-seeding can significantly change the conformation of other proteins, and this can also explain the generation of autoantibodies since such proteins would then be seen as not-self [22].

A chief consequence of the blockage of microcapillaries by fibrinolytic microclots is a slowing down of the blood flow, sometimes referred to (including by Virchow in his ‘triad’ [55–57]) as Blood Stasis. ‘Blood stasis’ is also a highly important concept in Traditional Asian Medicines (see e.g., [58–61]), and seems strongly correlated with the presence of fibrinolytic microclots [62]. Ischaemia or hypoxia are inevitable consequences, and indeed this property, leading to oxidative stress, is consequently common to all the chronic, inflammatory syndromes being considered here (e.g., [11,63–73]).

To date, the most frequent types of measurements of fibrinolytic microclots have mainly been ‘structural’ using thioflavin T staining and observation by fluorescence microscopy (e.g., [4,6,12,31,33,38,74]) or flow cytometry [32] (‘flow clotometry’ [34]). A more ‘functional’ assay would be highly desirable to complement this. Although many of the phenomena may occur deep inside the body, our chief focus here is on the human skin microcirculation [75] and its attendant disorders (e.g., [76–79]).

Capillaroscopy refers to a general technique that can potentially determine blood flow rates in the microcirculation in a simple and non-invasive manner, and, given the above, might potentially serve as an excellent functional assay for blood stasis and microclot presence. Sublingual microscopy [80], retinal [81], and nailfold capillaroscopy (NFC) are in

common use and—while other methods such as laser speckle contrast imaging [82–88] and thermography [89,90] may also be used—we focus here on NFC. To this end, the chief purpose of the present review is to develop the idea that NFC, including in particular its derivative nailfold videocapillaroscopy (NVC), will be of value in understanding syndromes in which fibrinoid microclots are involved, and to provide the evidence-based reasoning for this. A preprint has been lodged [91].

2. Nailfold Capillaroscopy

2.1. History and Modern Implementations

Capillaroscopy is a technique for looking at the microcirculation [75]. The idea that the study of capillaries might have disease-diagnostic value goes back to the 17th Century, when Johan Christophorous Kolhaus used a primitive microscope to observe the small blood vessels surrounding the nails, and later Giovanni Rasori, using a magnifying glass, related the observed properties to conjunctival inflammation [92]. A list of recent reviews is given in Table 1.

Modern microscopes, commonly using 200× magnification, coupled to well engineered illumination and focusing optics, are all that is necessary to acquire static (capillaroscopy) and dynamic (videocapillaroscopy) images, with a second element being how these images are interpreted—manually or computationally—to provide useful diagnostic information (Figure 2). Because our focus lies on the relationship with fibrinoid microclots, we do not provide detailed analyses of the precise procedures involved (e.g., [93–95]). Many commercial systems are available, although we neither seek to discriminate among them nor recommend particular models. They provide interfaces with laptops and even cellphones. Since interpretation by the human eye alone is neither straightforward nor objective [96,97], the more refined instrumentation usually comes with software to assist or even provide interpretation. It typically costs a few hundred pounds for entry-level models. Parameters (strictly, variables) that are measured or calculated include capillary density [98,99] and percentage of abnormal and giant capillaries, tortuosities, and haemorrhages [94,97,100–103]. EULAR (The European League Against Rheumatism) has agreed on a consented standardised capillaroscopic description protocol [93,104–107].

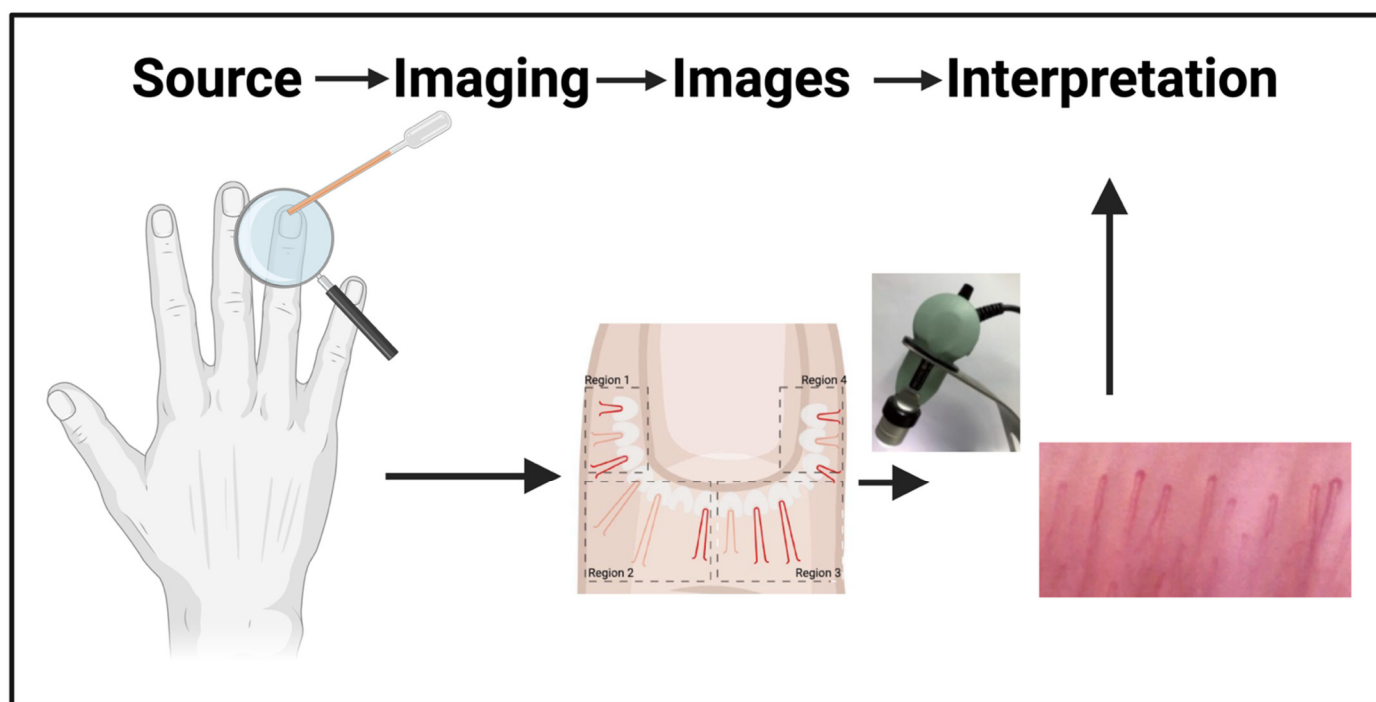


Figure 2. Cartoon illustrating the basic steps in nailfold capillaroscopy. Image includes elements of the Open Access (CC-BY 4.0) materials at [94,100,108]. The three fingers adjacent to the thumb may be profiled, with 4 regions on each [100]. The normal or healthy pattern (as illustrated) displays a regular architecture with uniform distribution and diameter and a hairpin shape [109].

Figure 2 also illustrates the kinds of capillary structure seen in healthy controls (and see e.g., [75,94,110]). Figure 3 provides a feel for the kinds of images that are obtainable under different conditions.

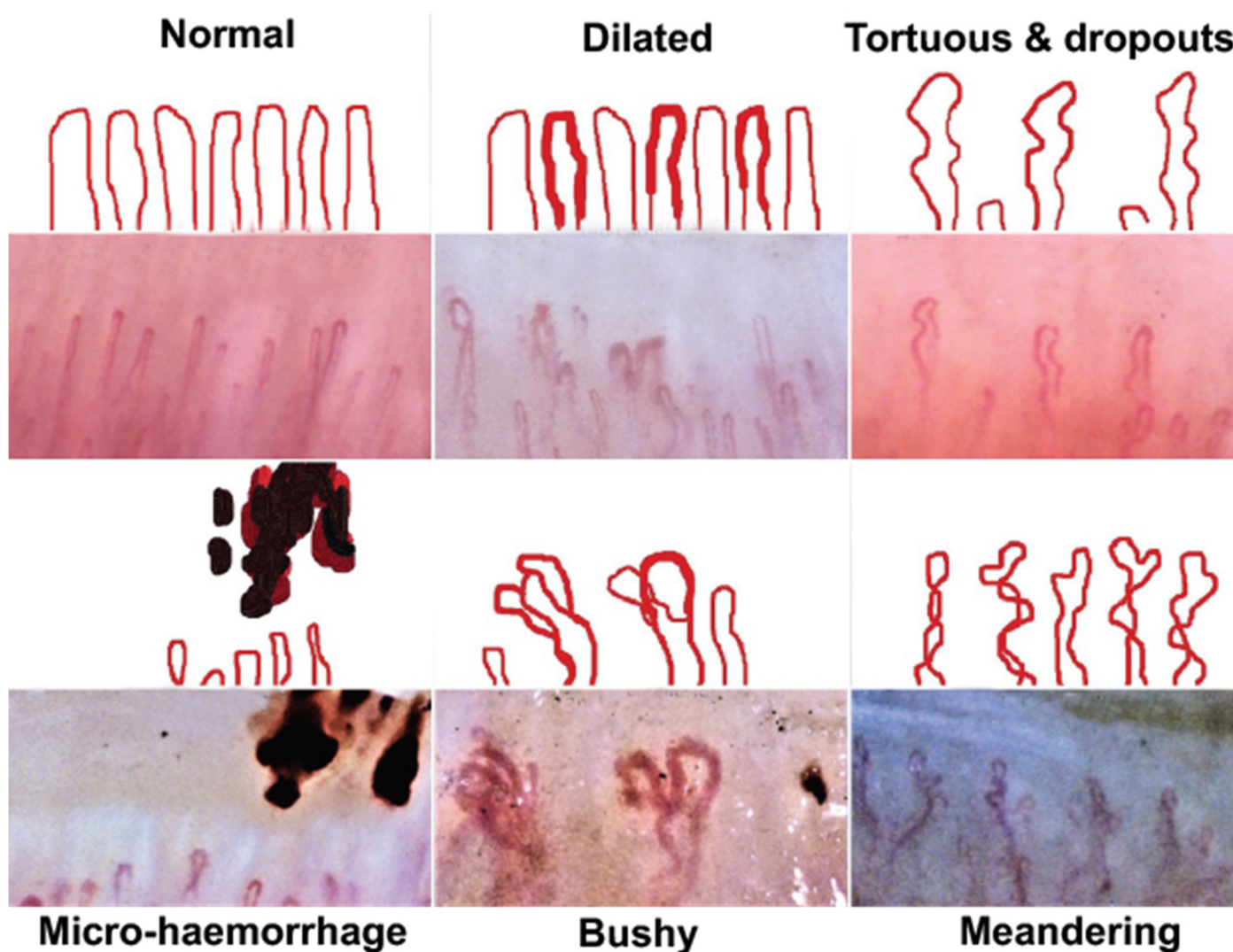


Figure 3. Some images and explanatory cartoons of various nailfold capillary morphologies. Taken from the CC-BY 4.0 Open Access paper [94].

Clearly, the strategy is generic, and while possibly the majority of studies have focused on Raynaud's disease, rheumatology, and systemic sclerosis (scleroderma), the range is very wide. This is partly because many are chronic inflammatory diseases with common vascular causes and/or symptoms [11], including endothelial dysfunction. Systemic sclerosis is recognised as a vascular disease involving endothelial dysfunction [111–117], thus bearing significant similarities to COVID-19 [118] that most certainly does [36,119–125], so it is not surprising that such commonalities exist. In a sense, this survey thus adds weight to the view that there are common co-occurrences of various symptoms. The advantage of nailfold capillaroscopy over, e.g., cytokine-based assessment of inflammation is that capillaroscopy is non-invasive, quick, and cheap, providing useful information for diagnosis and treatment. To illustrate its broad general utility, a sample of such studies in which it has been used is included in Table 1. While these are seen mostly as immunological in character, we recognise that the symptoms of many other syndromes can be reflected in the microcirculation. Specifically, Table 1 has three purposes. These are to show readers (i) that every disease where microclots have been measured shows abnormalities in the microcirculation as judged by NFC/NVC, (ii) for the microclot community to see how widespread and valuable the usage of NFC/NVC is and thus to encourage them to try it, and (iii) to point the NFC/NVC community at other diseases where (based on microclot measurements) we suggest their methods would be of value.

Table 1. Some disorders involving the microcirculation in which (mainly) nailfold (video) capillaroscopy has been found to have diagnostic utility or where fibrinoid microclots have been demonstrated. Disorders in which fibrinoid microclots have been demonstrated are rendered in **bold face**; note that every disorder in which microclots have been demonstrated has anomalies as assessed using nailfold capillaroscopy.

Disease or Syndrome	Comments	Selected Nailfold Capillaroscopy References	Selected Fibrinoid Microclot References (Where Tested)
Acute COVID-19	Capillary tortuosity, meandering, haemosiderin deposition, and microhaemorrhage increased; capillary density and length, and blood flow decreased	[126–138]	[18,29,139–142]
Alzheimer’s dementia	Greater nailfold capillary tortuosity in individuals with Alzheimer’s dementia	[143,144]	[12–14,145,146]
Anderson-Fabry disease	Also known as Fabry disease. Promising but underexplored. Subclasses detected depend on the α -galactosidase A variant.	[147–150]	
Anorexia nervosa	Related to connective tissue disorders	[151,152]	
Antineutrophil Cytoplasmic Antibody-Associated (ANCA) Vasculitis	Neoangiogenesis, capillary loss, microhaemorrhages, and bushy and enlarged capillaries	[153–156]	
Atopic dermatitis	Many more lesions, e.g., pitting, capillary density, tortuosity	[157]	
Behçet’s disease	Increases in capillary dilatation, tortuous and branched capillaries, and microhaemorrhages	[158,159]	
Biliary cirrhosis	Multiple abnormalities	[160]	
Cancer	Not yet widely deployed, but some suggestive data imply it could have diagnostic or prognostic value.	[161]	
Chronic obstructive pulmonary disorder (COPD)	Review	[162] (but cf. [163])	
Chronic smokers	Abnormalities are more common in chronic smokers	[164]	
Chronic urticaria	Lower capillary density, more capillary malformations, and more irregular capillary dilations	[165]	
Connective tissue disorders	Various	[166–168]	
Coronary heart disease	Assessment of capillary blood flow and relation to erythrocyte aggregation	[169]	
Dermatomyositis	Diminished capillary density and abnormal capillary morphology (including enlargement) in patients. It can be related to antibody levels. Haemosiderin deposits can occur.	[104,170–179]	
Diabetes mellitus, type 1	General	[180,181]	
	Use of deep learning	[182]	
Diabetes mellitus, type 2	Capillary dilatation, avascular zones, and tortuous capillaries	[183–185]	[12,17,18,186,187]
	Peak capillary blood flow velocity (CBFV) post-occlusion is much lower	[188]	
	Use of deep learning	[182]	

	Changes closely related to the quality of glucose control	[189,190]	
	Capillaries are larger but less dense	[191]	
	Various differences	[192,193]	
Diabetic complications	Listed separately below		
Diabetic foot	Significant difference in pulp of the big toe	[194]	
Diabetic nephropathy	Significant correlation between lowered glomerular filtration rate and e.g., reduced fundus transparency and visibility of the sub-venous plexus	[195,196]	
Diabetic neuropathy	Improved by α -lipoic acid	[197]	
Diabetic retinopathy	Decreased capillary length, width, number, and turbidity, crossing capillaries, and other abnormalities	[183,184,198–201]	
Digital ulcers	A common accompaniment to systemic sclerosis and Raynaud's disease	[202–204]	
Endothelial dysfunction	Reviews	[117,128]	[125]
	In livedoid vasculopathy	[205]	
	Association with rheumatoid arthritis	[206]	
Fibromyalgia	Raynaud's disease and impaired microvascular function are common in patients with fibromyalgia, where nailfold abnormalities are common.	[207–210]	
	Fewer capillaries, apical limb width, and capillary width decreased	[78,211]	See [44], and for amyloid deposition in skeletal muscle [212]
	Mean capillary loop diameter, micro-aneurysm number, avascular areas, and neoangiogenic capillaries significantly higher	[213]	
Gaucher disease	Various subtypes. Microangiopathy is the most obvious NFC finding	[214]	
General reviews		[77,94,100,215–217]	
	Non-rheumatic diseases	[218]	
	Vascular disease	[219]	
Glaucoma	Huge decrease in capillary blood flow	[220]	
Heart failure	Greater abnormalities with preserved ejection fraction	[221]	
Hepatitis, viral	Changes in the avascular area, capillary dilatation, capillary tortuosity, and capillary enlargement were observed	[222]	
Hypertension (general)	Many differences, including lowered capillary density and other morphological changes	[223]	
Idiopathic inflammatory myopathy	Significant differences, including between subtypes	[224–228]	
Idiopathic macular telangiectasia type 2	Increased capillary tortuosity, 'bizarre' capillaries, and microhaemorrhage in the patient group compared to the controls	[229]	
Leprosy	Capillary dropouts are the most frequent, followed by tortuous, receding, and dilated capillaries	[230]	
Long COVID	Compares Long COVID patients without and with systemic sclerosis. Long COVID patients show more microvascular alterations than recovered COVID	[231]	[21,24,30–35,43,45,125,232]

	patients.		
Lupus (systemic lupus erythematosus)		[105,173,233–236]	
Migraine	Seemingly little studied recently by nailfold capillaroscopy, but major differences observed vs controls, especially when cold-induced	[237,238]	[239]
Neutropenia	Indirect assessment from videocapillaroscopy	[240,241]	
Obstructive sleep apnoea	All capillaroscopy findings were significantly higher in the patient group	[242]	
Parkinson's disease	Seemingly not yet studied by nailfold capillaroscopy in any detail.		[12,16,243]
Polycythemia vera	Increase in the diameter of vessels	[244]	
Polymyositis	Scleroderma pattern predominated and improved after treatment.	[104,170,179,245,246]	
Pre-eclampsia	Change in capillary length and density with pregnancy-induced hypertension, whether pre-eclamptic or not. Some relationship to maternal blood pressure [247].	[248]	
	Decreased capillary density in pre-eclampsics	[249]	
	Review of capillaroscopy in pregnancy	[250]	
Psoriasis		[251–257]	
Pulmonary arterial hypertension	(Can accompany systemic sclerosis.) Lowered capillary density	[223,258,259]	
Raynaud's disease or Raynaud's phenomenon	Common accompaniment of systemic sclerosis. NFC especially used in discriminating primary Raynaud's from secondary Raynaud's due to systemic sclerosis	[89,204,260–271]	
	Standardisation	[106]	
Rheumatology, especially rheumatoid arthritis	Reviews	[92,251,272–280]	[19,281,282]
Sarcoidosis	Early but promising	[283–285]	
Sarcopenia	Common in rheumatoid arthritis and systemic sclerosis	[286,287]	
Sepsis and septic shock	See Section 2.3	[288]	[38] and see [289]
	Decreased capillary density sublingually	[290]	
Sickle cell disease	Lower capillary density and more dilated capillaries	[291]	
Sjögren's syndrome		[292,293]	
Systemic sclerosis	It is increasingly seen as a vasculopathy [114]. Reviews on the role of NFC are in the adjacent column. Arguably, the commonest area of study.	[107,172,294–309]	
	Use of the NEMO score (the number of microhaemorrhages plus micro-thromboses)	[310–312]	
	Patients with primary biliary cholangitis	[313]	
	Differences when pulmonary arterial hypertension is also present	[314,315]	

The widespread occurrence of alterations in the microcirculation, as judged by nailfold capillaroscopy, shows how extensive this is in multiple syndromes that plausibly share common causes. The important point here is that, where tested, all examples in which fibrinoid microclots have been measured in plasma also show microcirculation disorders, as one would expect.

One reviewer questioned whether these techniques, that are well accepted for their ability to measure the morphological properties of microcapillaries, are also suitable for measuring blood **flow**; clearly individual static images can not do that directly, although it is pretty obvious (given that these methods are routinely used for assessing the **microcirculation**) that changes in capillary diameter and tortuosity necessarily have such effects [107,143,144,217,273,315,316]. Equally clearly, video methods that image capillaries at intervals and with a suitable magnification can precisely detect the flow of blood, as the following illustrative references that demonstrate it explicitly amply show (e.g., [100,117,143,168,188,217,317–326]). This does not seem remotely controversial.

2.2. Long COVID as an Example

Following infection with the SARS-CoV-2 virus, a significant fraction of individuals fail to return fully to health, and after three months are said to suffer from post-acute sequelae of COVID-19 (PASC), commonly known as Long COVID [327]. Long COVID is estimated to affect or have affected over 400 million individuals worldwide, contributing to an annual economic burden of \$1 trillion or ~1% of the global economy [328,329]. Symptoms vary widely [330–335], with fatigue being the most common [336,337]. It is a disease in which many studies have shown the presence of fibrinoid microclots [21,24,30–35,43,45,125,232], which provide ready explanations for the various symptoms [21,22,42,43]. Importantly, Cutolo and colleagues carried out a valuable study [231] using NFC in patients with Long COVID and matched controls. Specifically, nailfold videocapillaroscopy (NVC) showed significant microvascular damage in long covid (LC) patients compared with matched healthy controls. Dilated capillaries, microhaemorrhages, abnormal shapes, and reduced capillary density were detectable in LC patients even 12 months after acute SARS-CoV-2 infection. Importantly, NVC demonstrated that these observables were normalised in patients who had recovered. It would seem that NVC is a valuable functional diagnostic for individuals with Long COVID, and a potentially valuable complement to the measurement of fibrinoid microclots.

2.3. Sepsis and Septic Shock

Sepsis and septic shock are of special interest here for a number of reasons. First, they can be highly dangerous. Secondly, they are accompanied by microthrombi [338] that we suggested are our fibrinoid microclots [289], and thirdly, the fibrinoid microclot burden, as now so measured, is highly predictive of survival in the ICU (odds ratio > 5) [38]. (The microclots are even more predictive of disseminated intravascular coagulation [38].) Finally, the microcirculation (Figure 4) is intimately involved in sepsis and septic shock.

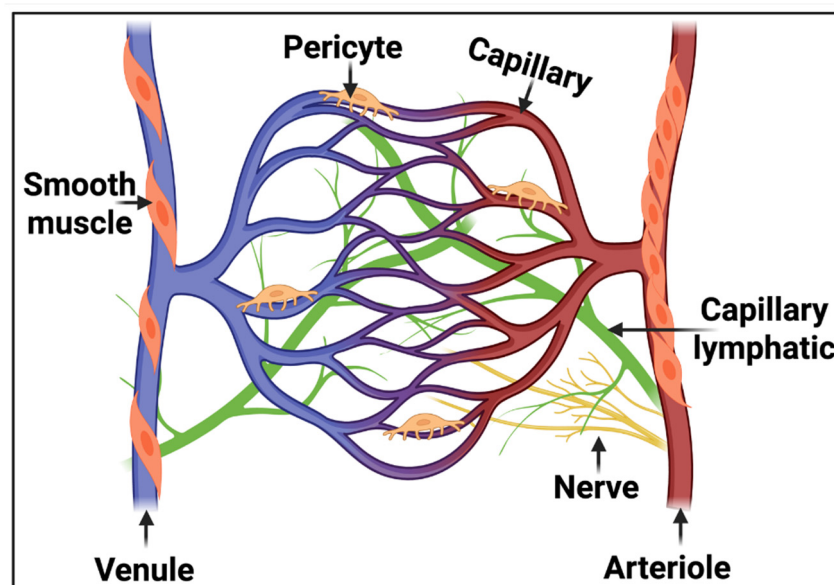


Figure 4. The anatomy of the microcirculation is the largest part of the vascular system and consists of the smallest vessels, referred to as arterioles, capillaries, and venules. The lymphatic capillaries carry the extravascular fluid into the venous system, while the

arterioles are surrounded by vascular smooth muscle cells responsible for regulating arteriole tone. Taken and slightly adapted from the CC-BY 4.0 publication [339].

Specifically, disorders of the endothelium and microcirculation leading to hypoxia are recognised as an intimate part of sepsis and septic shock (e.g., [288,340–363]). However, NFC is said to be not much used as the nailfold vascular bed is sensitive to peripheral vasoconstriction, vasopressor agents, and temperature changes. None of these seems like insurmountable issues [364], and it would seem that the recognition of the importance of both the microcirculation and fibrinoid microclots in sepsis mortality warrants a far more detailed analysis, to include a comparison between microclot burden, nailfold capillaroscopic findings, any effects of clotbusters or other treatments, and disease outcomes. Indeed, the generally less common sublingual capillaroscopy is known to be very useful [365] and even predictive of mortality [366].

2.4. 'Blood Stasis' and Treatments to Improve It

As mentioned above, 'Blood stasis', a term used as part of Virchow's triad [55–57,367,368], is an extremely important concept in Traditional Chinese Medicine [58,369–375] (known there as Xue Yu (血瘀) [376]). Exactly equivalent ideas exist in Japanese Kampo medicine (where it is termed Oketsu [377–380]) and in Traditional Korean Medicine (where blood stasis is known as 'Ouhyl' or 'Eohyl') [61,381]). We recently summarised the extensive evidence to the effect that 'blood stasis' is precisely a manifestation of the presence and effects of fibrinoid microclots [62], in that all syndromes known to display fibrinoid microclots are considered to be diseases of blood stasis. While such traditional medical formalisms also recognise that one should treat the patient as an individual, standard herbal formulas for diseases of blood stasis do exist, in the form of XueFu ZhuYu [62,382–387] and Keishibukuryogan [377,388,389], and are known to improve the microcirculation. Consequently, it would be of considerable interest to assess this via nailfold capillaroscopy.

2.5. Future Directions

Although many of the commercial systems are served by reasonably sophisticated software to assist interpretation [390], much of the downstream analysis remains in the hands and minds of skilled clinicians, and, especially depending on the image quality [391], is necessarily subjective [323,392–394]. This said, where it has been studied inter-rater reliability has been found to be good (e.g., [92,96,392,395,396]). An easy prediction is that these kinds of tasks will soon be taken over by intelligent systems trained using modern data-driven generative methods of machine learning, commonly referred to as artificial intelligence or 'AI'. This particular revolution is, of course, already underway [390,393,394,397–405]. To date, the lack of availability of labelled datasets has confined most efforts to transfer learning or 'fine tuning' of other models [406]. However, much as with equivalent developments in general image processing [407,408], chemistry [409], and protein science [410–412], progress will be greatly assisted [275] by the availability of a database of tagged images, videos and appropriate metadata taken directly from nailfold capillaroscopy, as well as the ability [413] to explain the bases (in terms of features extracted) for any such disease classifications.

A further point is that while many diseases have been studied using nailfold capillaroscopy (Table 1), there are quite a number more, some with high prevalence, that have not. These would seem to offer considerable opportunities for devising analyses with prognostic value. For instance, myalgic encephalopathy/chronic fatigue syndrome (ME/CFS) shares many of the hallmarks of the other diseases (including Long COVID) listed in Table 1 [414–416], including endothelial dysfunction [37,417–420], fibrinoid microclots [23,37,421], and a disrupted microcirculation [422] (as in Figure 5), but we know of no attempt to assess its severity using nailfold capillaroscopy, which would provide further evidence beyond that existing (see [232]) for a deranged microcirculation in this syndrome.

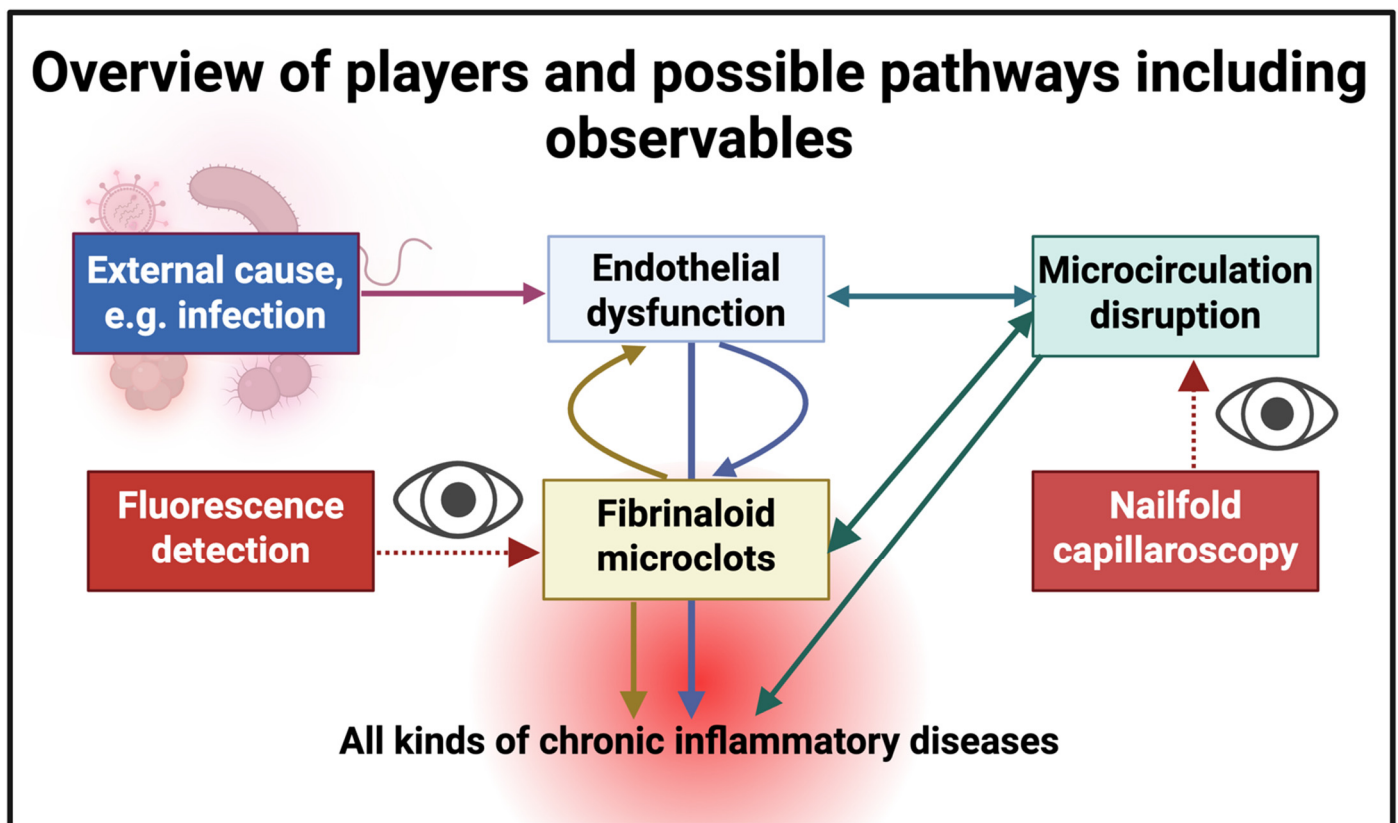


Figure 5. Cartoon illustrating the systems aspects of the main features of this prospective review. Endothelial dysfunction, the result of a deterministic ‘external’ cause such as (a new or reactivated) infection, trauma, or stress, leads to the disruption of the microcirculation and to fibrinoid microclots, each of which can potentially exacerbate the others. Our focus here is on nailfold capillaroscopy, though we have rehearsed the methods for microclot detection. Endothelial (dys)function *in vivo* is commonly assessed via flow-mediated dilatation [117,423] or various biomarkers (e.g., [424–427]). We anticipate that the combination of all three will be especially powerful in understanding the nature and severity of these kinds of disease, thereby assessing mechanisms and candidate treatments.

This review has purposely confined itself to nailfold capillaroscopy since relatively inexpensive equipment to implement the method is widely available. This said, we recognise that more sophisticated methods will likely provide much more power. 3D optoacoustic imaging (raster scanning optoacoustic mesoscopy) [428–430] is one such approach, mirroring (in a certain sense) the developments [431–435] in optoacoustic infrared and Raman spectroscopy and imaging. Another trend towards using smart phones is taking photographs directly to assess digital lesions [436–438].

3. Conclusions

The novelty of this synthetic review (see [439]) lies in bringing together two fields that have until now pursued entirely separate paths, namely the fields of fibrinoid microclot measurements and nailfold (video) capillaroscopy. Nailfold capillaroscopy and nailfold videocapillaroscopy enjoy widespread usage in a large number of syndromes involving vascular issues and/or autoimmunity where they manifest in the microcirculation (Table 1). However, until now, there has been no recognition of the possibility that changes in the static and especially the video images thereby observed might be related to the well-established presence of fibrinoid microclots in many of these diseases. We believe that the arguments deployed here now make a comparison of the prevalence of the ‘structural’ microclots in images seen in microscopy or imaging flow cytometry with the structural and importantly more ‘functional’ images observable by capillaroscopic assays a very worthwhile endeavour.

Author Contributions

Conceptualization, D.B.K. & E.P.; Formal Analysis, D.B.K. & E.P.; Resources, D.B.K. & E.P.; Writing—Original Draft Preparation, D.B.K.; Writing—Review & Editing, D.B.K. & E.P.; Visualization, D.B.K. & E.P.; Funding Acquisition, D.B.K. & E.P.

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Declaration of Competing Interest

EP is a named inventor on a patent disclosing the use of fluorescence microscopy in Long COVID.

References

1. Pretorius E, Oberholzer HM, van der Spuy WJ, Meiring JH. The changed ultrastructure of fibrin networks during use of oral contraception and hormone replacement. *J. Thromb. Thrombolysis* **2010**, *30*, 502–506. doi:10.1007/s11239-010-0502-4.
2. Pretorius E, Swanepoel AC, Oberholzer HM, van der Spuy WJ, Duim W, Wessels PF. A descriptive investigation of the ultrastructure of fibrin networks in thrombo-embolic ischemic stroke. *J. Thromb. Thrombolysis* **2011**, *31*, 507–513. doi:10.1007/s11239-010-0538-5.
3. Pretorius E, Vermeulen N, Bester J, Lipinski B, Kell DB. A novel method for assessing the role of iron and its functional chelation in fibrin fibril formation: the use of scanning electron microscopy. *Toxicol. Mech. Methods* **2013**, *23*, 352–359. doi:10.3109/15376516.2012.762082.
4. Pretorius E, Mbotwe S, Bester J, Robinson CJ, Kell DB. Acute induction of anomalous and amyloidogenic blood clotting by molecular amplification of highly substoichiometric levels of bacterial lipopolysaccharide. *J. R. Soc. Interface* **2016**, *123*, 20160539. doi:10.1098/rsif.2016.0539.
5. Kell DB, Pretorius E. Proteins behaving badly. Substoichiometric molecular control and amplification of the initiation and nature of amyloid fibril formation: lessons from and for blood clotting. *Progr. Biophys. Mol. Biol.* **2017**, *123*, 16–41. doi:10.1016/j.pbiomolbio.2016.08.006.
6. Pretorius E, Page MJ, Hendricks L, Nkosi NB, Benson SR, Kell DB. Both lipopolysaccharide and lipoteichoic acids potently induce anomalous fibrin amyloid formation: assessment with novel Amytracker™ stains. *J. R. Soc. Interface* **2018**, *15*, 20170941. doi:10.1098/rsif.2017.0941.
7. Biancalana M, Makabe K, Koide A, Koide S. Molecular mechanism of thioflavin-T binding to the surface of beta-rich peptide self-assemblies. *J. Mol. Biol.* **2009**, *385*, 1052–1063. doi:10.1016/j.jmb.2008.11.006.
8. Biancalana M, Koide S. Molecular mechanism of Thioflavin-T binding to amyloid fibrils. *Biochim. Biophys. Acta* **2010**, *1804*, 1405–1412. doi:10.1016/j.bbapap.2010.04.001.
9. Amdursky N, Erez Y, Huppert D. Molecular rotors: what lies behind the high sensitivity of the thioflavin-T fluorescent marker. *Acc. Chem. Res.* **2012**, *45*, 1548–1557. doi:10.1021/ar300053p.
10. Gade Malmos K, Blancas-Mejia LM, Weber B, Buchner J, Ramirez-Alvarado M, Naiki H, et al. ThT 101: a primer on the use of thioflavin T to investigate amyloid formation. *Amyloid* **2017**, *24*, 1–16. doi:10.1080/13506129.2017.1304905.
11. Kell DB, Pretorius E. No effects without causes. The Iron Dysregulation and Dormant Microbes hypothesis for chronic, inflammatory diseases. *Biol. Rev.* **2018**, *93*, 1518–1557. doi:10.1111/brv.12407.
12. de Waal GM, Engelbrecht L, Davis T, de Villiers WJS, Kell DB, Pretorius E. Correlative Light-Electron Microscopy detects lipopolysaccharide and its association with fibrin fibres in Parkinson's Disease, Alzheimer's Disease and Type 2 Diabetes Mellitus. *Sci. Rep.* **2018**, *8*, 16798. doi:10.1038/s41598-018-35009-y.
13. Pretorius E, Bester J, Kell DB. A bacterial component to Alzheimer-type dementia seen via a systems biology approach that links iron dysregulation and inflammagen shedding to disease. *J. Alzheimers. Dis.* **2016**, *53*, 1237–1256. doi:10.3233/JAD-160318.
14. Pretorius E, Bester J, Page MJ, Kell DB. The potential of LPS-binding protein to reverse amyloid formation in plasma fibrin of individuals with Alzheimer-type dementia. *Front. Aging Neurosci.* **2018**, *10*, 257. doi:10.3389/fnagi.2018.00257.
15. Adams B, Nunes JM, Page MJ, Roberts T, Carr J, Nell TA, et al. Parkinson's disease: a systemic inflammatory disease accompanied by bacterial inflammagens. *Front. Aging Neurosci.* **2019**, *11*, 210. doi:10.3389/fnagi.2019.00210.
16. Pretorius E, Page MJ, Mbotwe S, Kell DB. Lipopolysaccharide-binding protein (LBP) can reverse the amyloid state of fibrin

- seen or induced in Parkinson's disease. *PLoS ONE* **2018**, *13*, e0192121. doi:10.1371/journal.pone.0192121.
17. Pretorius E, Page MJ, Engelbrecht L, Ellis GC, Kell DB. Substantial fibrin amyloidogenesis in type 2 diabetes assessed using amyloid-selective fluorescent stains. *Cardiovasc. Diabetol.* **2017**, *16*, 141. doi:10.1186/s12933-017-0624-5.
 18. Pretorius E, Venter C, Laubscher GJ, Lourens PJ, Steenkamp J, Kell DB. Prevalence of readily detected amyloid blood clots in 'unclothed' Type 2 Diabetes Mellitus and COVID-19 plasma: A preliminary report. *Cardiovasc. Diabetol.* **2020**, *19*, 193. doi:10.1186/s12933-020-01165-7.
 19. Pretorius E, Akeredolu O-O, Soma P, Kell DB. Major involvement of bacterial components in rheumatoid arthritis and its accompanying oxidative stress, systemic inflammation and hypercoagulability. *Exp. Biol. Med.* **2017**, *242*, 355–373. doi:10.1177/1535370216681549.
 20. Kell DB, Pretorius E. The simultaneous occurrence of both hypercoagulability and hypofibrinolysis in blood and serum during systemic inflammation, and the roles of iron and fibrin(ogen). *Integr. Biol.* **2015**, *7*, 24–52. doi:10.1039/c4ib00173g.
 21. Kell DB, Laubscher GJ, Pretorius E. A central role for amyloid fibrin microclots in long COVID/PASC: origins and therapeutic implications. *Biochem. J.* **2022**, *479*, 537–559. doi:10.1042/BCJ20220016.
 22. Kell DB, Pretorius E. Are fibrinoid microclots a cause of autoimmunity in Long Covid and other post-infection diseases? *Biochem. J.* **2023**, *480*, 1217–1240. doi:10.1042/BCJ20230241.
 23. Nunes JM, Kruger A, Proal A, Kell DB, Pretorius E. The occurrence of hyperactivated platelets and fibrinoid microclots in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). *Pharmaceuticals* **2022**, *15*, 931. doi:10.3390/ph15080931.
 24. Turner S, Khan MA, Putrino D, Woodcock A, Kell DB, Pretorius E. Long COVID: pathophysiological factors and abnormal coagulation. *Trends Endocrinol. Metab.* **2023**, *34*, 321–344. doi:10.1016/j.tem.2023.03.002.
 25. Kell DB, Lip GYH, Pretorius E. Fibrinoid Microclots and Atrial Fibrillation. *Biomedicines* **2024**, *12*, 891. doi:10.3390/biomedicines12040891.
 26. Klingstedt T, Shirani H, Åslund KOA, Cairns NJ, Sigurdson CJ, Goedert M, et al. The structural basis for optimal performance of oligothiophene-based fluorescent amyloid ligands: conformational flexibility is essential for spectral assignment of a diversity of protein aggregates. *Chemistry* **2013**, *19*, 10179–10192. doi:10.1002/chem.201301463.
 27. Nilsson KP, Lindgren M, Hammarström P. A pentameric luminescent-conjugated oligothiophene for optical imaging of in vitro-formed amyloid fibrils and protein aggregates in tissue sections. *Methods Mol. Biol.* **2012**, *849*, 425–434. doi:10.1007/978-1-61779-551-0_29.
 28. Stepanchuk A, Tahir W, Nilsson KPR, Schatzl HM, Stys PK. Early detection of prion protein aggregation with a fluorescent pentameric oligothiophene probe using spectral confocal microscopy. *J. Neurochem.* **2021**, *156*, 1033–1048. doi:10.1111/jnc.15148.
 29. Laubscher GJ, Lourens PJ, Venter C, Kell DB, Pretorius E. TEG®, Microclot and Platelet Mapping for Guiding Early Management of Severe COVID-19 Coagulopathy. *J. Clin. Med.* **2021**, *10*, 5381. doi:10.3390/jcm10225381.
 30. Pretorius E, Vlok M, Venter C, Bezuidenhout JA, Laubscher GJ, Steenkamp J, et al. Persistent clotting protein pathology in Long COVID/ Post-Acute Sequelae of COVID-19 (PASC) is accompanied by increased levels of antiplasmin. *Cardiovasc. Diabetol.* **2021**, *20*, 172. doi:10.1186/s12933-021-01359-7.
 31. Pretorius E, Venter C, Laubscher GJ, Kotze MJ, Oladejo S, Watson LR, et al. Prevalence of symptoms, comorbidities, fibrin amyloid microclots and platelet pathology in individuals with Long COVID/ Post-Acute Sequelae of COVID-19 (PASC). *Cardiovasc. Diabetol.* **2022**, *21*, 148. doi:10.1186/s12933-022-01579-5.
 32. Turner S, Laubscher GJ, Khan MA, Kell DB, Pretorius E. Accelerating discovery: A novel flow cytometric method for detecting fibrin(ogen) amyloid microclots using long COVID as a model. *Heliyon* **2023**, *9*, e19605. doi:10.1016/j.heliyon.2023.e19605.
 33. Dalton CF, de Oliveira MIR, Stafford P, Peake N, Kane B, Higham A, et al. Increased fibrinoid microclot counts in platelet-poor plasma are associated with Long COVID. *medRxiv* **2024**, 2024-04. doi:10.1101/2024.04.04.24305318.
 34. Pretorius E, Nunes M, Pretorius J, Kell DB. Flow Clotometry: Measuring Amyloid Microclots in ME/CFS, Long COVID, and Healthy Samples with Imaging Flow Cytometry. Research Square. 2024. Available online: <https://www.researchsquare.com/article/rs-4507472/v4507471> (accessed on 18 July 2025).
 35. Pretorius E, Thierry A, Sanchez C, Ha T, Pastor B, Mirandola A, et al. Circulating Microclots Are Structurally Associated with Neutrophil Extracellular Traps and Their Amounts Are Strongly Elevated in Long COVID Patients. Research Square. 2024. Available online: <https://www.researchsquare.com/article/rs-4666650/v4666651> (accessed on 18 July 2025).
 36. Turner S, Naidoo CA, Usher TJ, Kruger A, Venter C, Laubscher GJ, et al. Increased levels of inflammatory and endothelial biomarkers in blood of long COVID patients point to thrombotic endothelialitis. *Semin. Thromb. Hemost.* **2024**, *50*, 288–294. doi:10.1055/s-0043-1769014.
 37. Nunes JM, Kell DB, Pretorius E. Cardiovascular and haematological pathology in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): a role for Viruses. *Blood Rev.* **2023**, *60*, 101075. doi:10.1016/j.blre.2023.101075.
 38. Schofield J, Abrams ST, Jenkins R, Lane S, Wang G, Toh CH. Microclots, as defined by amyloid-fibrinogen aggregates, predict risks of disseminated intravascular coagulation and mortality. *Blood Adv.* **2024**, *8*, 2499–2508. doi:10.1182/bloodadvances.2023012473.

39. Marfella R, Prattichizzo F, Sardu C, Fulgenzi G, Graciotti L, Spadoni T, et al. Microplastics and nanoplastics in atheromas and cardiovascular events. *N. Engl. J. Med.* **2024**, *390*, 900–910. doi:10.1056/NEJMoa2309822.
40. Wang S, Lu W, Cao Q, Tu C, Zhong C, Qiu L, et al. Microplastics in the Lung Tissues Associated with Blood Test Index. *Toxics* **2023**, *11*, 759. doi:10.3390/toxics11090759.
41. Zhao B, Rehati P, Yang Z, Cai Z, Guo C, Li Y. The potential toxicity of microplastics on human health. *Sci. Total Environ.* **2024**, *912*, 168946. doi:10.1016/j.scitotenv.2023.168946.
42. Kell DB, Pretorius E. The potential role of ischaemia-reperfusion injury in chronic, relapsing diseases such as rheumatoid arthritis, long COVID and ME/CFS: evidence, mechanisms, and therapeutic implications. *Biochem. J.* **2022**, *479*, 1653–1708. doi:10.1042/BCJ20220154.
43. Kell DB, Khan MA, Kane B, Lip GYH, Pretorius E. Possible role of fibrinoid microclots in Postural Orthostatic Tachycardia Syndrome (POTS): focus on Long COVID. *J. Pers. Med.* **2024**, *14*, 170. doi:10.3390/jpm14020170.
44. Kell DB, Pretorius E. Potential Roles of Fibrinoid Microclots in Fibromyalgia Syndrome. OSF Preprint. 2024. Available online: <https://osf.io/9e2y5/> (accessed on 18 July 2025).
45. Kruger A, Vlok M, Turner S, Venter C, Laubscher GJ, Kell DB, et al. Proteomics of fibrin amyloid microclots in Long COVID/Post-Acute Sequelae of COVID-19 (PASC) shows many entrapped pro-inflammatory molecules that may also contribute to a failed fibrinolytic system. *Cardiovasc. Diabetol.* **2022**, *21*, 190. doi:10.1186/s12933-022-01623-4.
46. Kell DB, Pretorius E. Proteomic evidence for amyloidogenic cross-seeding in fibrinoid microclots. *Int. J. Mol. Sci.* **2024**, *25*, 10809. doi:10.3390/ijms251910809.
47. Ząbczyk M, Stachowicz A, Natowska J, Olszanecki R, Wiśniewski JR, Undas A. Plasma fibrin clot proteomics in healthy subjects: relation to clot permeability and lysis time. *J. Proteom.* **2019**, *208*, 103487. doi:10.1016/j.jprot.2019.103487.
48. Kell DB, Pretorius E. The proteome content of blood clots observed under different conditions: Successful role in predicting clot amyloid(ogenicity). *Molecules* **2025**, *30*, 668. doi:10.3390/molecules30030668.
49. Kell DB, Doyle KM, Salcedo-Sora E, Sekhar A, Walker M, Pretorius E. AmyloGram reveals amyloidogenic potential in stroke thrombus proteomes. *bioRxiv* **2025**, 2025-07. doi:10.1101/2025.07.07.663482.
50. Pretorius E, Windberger UB, Oberholzer HM, Auer RE. Comparative ultrastructure of fibrin networks of a dog after thrombotic ischaemic stroke. *Onderstepoort J. Vet. Res.* **2010**, *77*, E1–E4. doi:10.4102/ojvr.v77i1.4.
51. Pretorius E, Steyn H, Engelbrecht M, Swanepoel AC, Oberholzer HM. Differences in fibrin fiber diameters in healthy individuals and thromboembolic ischemic stroke patients. *Blood Coagul. Fibrinolysis* **2011**, *22*, 696–700. doi:10.1097/MBC.0b013e32834bdb32.
52. Pretorius E. The use of a desktop scanning electron microscope as a diagnostic tool in studying fibrin networks of thromboembolic ischemic stroke. *Ultrastruct. Pathol.* **2011**, *35*, 245–250. doi:10.3109/01913123.2011.606659.
53. Grixti JM, Chandran A, Pretorius JH, Walker M, Sekhar A, Pretorius E, et al. The clots removed from ischaemic stroke patients by mechanical thrombectomy are amyloid in nature. *medRxiv* **2024**, 2024-11. doi:10.1101/2024.11.01.24316555.
54. Grixti JM, Chandran A, Pretorius JH, Walker M, Sekhar A, Pretorius E, et al. Amyloid presence in acute ischemic stroke thrombi: observational evidence for fibrinolytic resistance. *Stroke* **2025**, *56*, e165–e167. doi:10.1161/STROKEAHA.124.050033.
55. Bagot CN, Arya R. Virchow and his triad: a question of attribution. *Br. J. Haematol.* **2008**, *143*, 180–190. doi:10.1111/j.1365-2141.2008.07323.x.
56. Gonzalez-Gonzalez FJ, Ziccardi MR, McCauley MD. Virchow's Triad and the Role of Thrombosis in COVID-Related Stroke. *Front. Physiol.* **2021**, *12*, 769254. doi:10.3389/fphys.2021.769254.
57. Mehta JL, Calcaterra G, Bassareo PP. COVID-19, thromboembolic risk, and Virchow's triad: Lesson from the past. *Clin. Cardiol.* **2020**, *43*, 1362–1367. doi:10.1002/clc.23460.
58. Choi TY, Jun JH, Park B, Lee JA, You SS, Jung JY, et al. Concept of blood stasis in Chinese medical textbooks: A systematic review. *Eur. J. Integr. Med.* **2016**, *8*, 158–164. doi:10.1016/j.eujim.2015.09.137.
59. Huang H, Pan J, Han Y, Zeng L, Liang G, Yang W, et al. Chinese Herbal Medicines for Promoting Blood Circulation and Removing Blood Stasis for Preventing Deep Venous Thrombosis after Total Hip Arthroplasty: A Systematic Review and Meta-Analysis. *Comb. Chem. High. Throughput Screen.* **2021**, *24*, 893–907. doi:10.2174/1386207323666200901103732.
60. Li HQ, Wei JJ, Xia W, Li JH, Liu AJ, Yin SB, et al. Promoting blood circulation for removing blood stasis therapy for acute intracerebral hemorrhage: a systematic review and meta-analysis. *Acta Pharmacol. Sin.* **2015**, *36*, 659–675. doi:10.1038/aps.2014.139.
61. Park MS, Kim J, Kim KH, Yoo HR, Chae I, Lee J, et al. Modern concepts and biomarkers of blood stasis in cardio- and cerebrovascular diseases from the perspectives of Eastern and Western medicine: A scoping review protocol. *JBIM Evid. Synth.* **2023**, *21*, 214–222. doi:10.11124/JBIES-22-00020.
62. Kell DB, Pretorius E, Zhao H. A direct relationship between ‘blood stasis’ and fibrinoid microclots in chronic, inflammatory and vascular diseases, and some traditional natural products approaches to treatment. *Pharmaceuticals* **2025**, *18*, 712. doi:10.3390/ph18050712.
63. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, et al. Reactive oxygen species, toxicity, oxidative

- stress, and antioxidants: chronic diseases and aging. *Arch. Toxicol.* **2023**, *97*, 2499–2574. doi:10.1007/s00204-023-03562-9.
64. Biswas SK. Does the Interdependence between Oxidative Stress and Inflammation Explain the Antioxidant Paradox? *Oxid. Med. Cell Longev.* **2016**, *2016*, 5698931. doi:10.1155/2016/5698931.
 65. Fischer R, Maier O. Interrelation of oxidative stress and inflammation in neurodegenerative disease: role of TNF. *Oxid. Med. Cell Longev.* **2015**, *2015*, 610813. doi:10.1155/2015/610813.
 66. Gambini J, Stomsnes K. Oxidative Stress and Inflammation: From Mechanisms to Therapeutic Approaches. *Biomedicines* **2022**, *10*, 753. doi:10.3390/biomedicines10040753.
 67. Hussain T, Tan B, Yin Y, Blachier F, Tossou MCB, Rahu N. Oxidative Stress and Inflammation: What Polyphenols Can Do for Us? *Oxid. Med. Cell Longev.* **2016**, *2016*, 7432797. doi:10.1155/2016/7432797.
 68. Kell DB. Iron behaving badly: inappropriate iron chelation as a major contributor to the aetiology of vascular and other progressive inflammatory and degenerative diseases. *BMC Med. Genom.* **2009**, *2*, 2. doi:10.1186/1755-8794-2-2.
 69. Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, et al. Oxidative stress, aging, and diseases. *Clin. Interv. Aging* **2018**, *13*, 757–772. doi:10.2147/CIA.S158513.
 70. McGarry T, Biniecka M, Veale DJ, Fearon U. Hypoxia, oxidative stress and inflammation. *Free Radic. Biol. Med.* **2018**, *125*, 15–24. doi:10.1016/j.freeradbiomed.2018.03.042.
 71. Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB. Oxidative stress, inflammation, and cancer: How are they linked? *Free Radic. Biol. Med.* **2010**, *49*, 1603–1616. doi:10.1016/j.freeradbiomed.2010.09.006.
 72. Siti HN, Kamisah Y, Kamsiah J. The role of oxidative stress, antioxidants and vascular inflammation in cardiovascular disease (a review). *Vascul Pharmacol.* **2015**, *71*, 40–56. doi:10.1016/j.vph.2015.03.005.
 73. Zhazykbayeva S, Pabel S, Mugge A, Sossalla S, Hamdani N. The molecular mechanisms associated with the physiological responses to inflammation and oxidative stress in cardiovascular diseases. *Biophys. Rev.* **2020**, *12*, 947–968. doi:10.1007/s12551-020-00742-0.
 74. Grixti JM, Theron CW, Salcedo-Sora JE, Pretorius E, Kell DB. Automated microscopic measurement of fibrinoid microclots and their degradation by nattokinase, the main natto protease. *J. Exp. Clin. Appl. Chin. Med.* **2024**, *5*, 30–55. doi:10.62767/jecacm504.6557.
 75. Cracowski JL, Roustit M. Human Skin Microcirculation. *Compr. Physiol.* **2020**, *10*, 1105–1154. doi:10.1002/cphy.c190008.
 76. Jung F, Pindur G, Ohlmann P, Spitzer G, Sternitzky R, Franke RP, et al. Microcirculation in hypertensive patients. *Biorheology* **2013**, *50*, 241–255. doi:10.3233/BIR-130645.
 77. Jung C, Kelm M. Evaluation of the microcirculation in critically ill patients. *Clin. Hemorheol. Microcirc.* **2015**, *61*, 213–224. doi:10.3233/CH-151994.
 78. Morf S, Amann-Vesti B, Forster A, Franzeck UK, Koppensteiner R, Uebelhart D, et al. Microcirculation abnormalities in patients with fibromyalgia—measured by capillary microscopy and laser fluxmetry. *Arthritis Res. Ther.* **2005**, *7*, R209–R216. doi:10.1186/ar1459.
 79. Lutze S, Westphal T, Jünger M, Arnold A. Microcirculation disorders of the skin. *J. Dtsch. Dermatol. Ges.* **2024**, *22*, 236–264. doi:10.1111/ddg.15242.
 80. Radic M, Thomas J, McMillan S, Frech T. Does sublingual microscopy correlate with nailfold videocapillaroscopy in systemic sclerosis? *Clin. Rheumatol.* **2021**, *40*, 2263–2266. doi:10.1007/s10067-020-05495-5.
 81. Jakhar D, Grover C, Singal A, Das GK. Nailfold Capillaroscopy and Retinal Findings in Patients with Systemic Sclerosis: Is There An Association? *Indian. Dermatol. Online J.* **2020**, *11*, 382–386. doi:10.4103/idoj.IDOJ_264_19.
 82. Briers D, Duncan DD, Hirst E, Kirkpatrick SJ, Larsson M, Steenbergen W, et al. Laser speckle contrast imaging: theoretical and practical limitations. *J. Biomed. Opt.* **2013**, *18*, 066018. doi:10.1117/1.JBO.18.6.066018.
 83. Couturier A, Bouvet R, Cracowski JL, Roustit M. Reproducibility of high-resolution laser speckle contrast imaging to assess cutaneous microcirculation for wound healing monitoring in mice. *Microvasc. Res.* **2022**, *141*, 104319. doi:10.1016/j.mvr.2022.104319.
 84. Hellmann M, Kalinowski L, Cracowski JL. Laser speckle contrast imaging to assess microcirculation. *Cardiol. J.* **2022**, *29*, 1028–1030. doi:10.5603/CJ.a2022.0097.
 85. Lazaridis A, Triantafyllou A, Mastrogiannis K, Malliora A, Doumas M, Gkaliagkousi E. Assessing skin microcirculation in patients at cardiovascular risk by using laser speckle contrast imaging. A narrative review. *Clin. Physiol. Funct. Imaging* **2023**, *43*, 211–222. doi:10.1111/cpf.12819.
 86. Linkous C, Pagan AD, Shope C, Andrews L, Snyder A, Ye T, et al. Applications of Laser Speckle Contrast Imaging Technology in Dermatology. *JID Innov.* **2023**, *3*, 100187. doi:10.1016/j.xjidi.2023.100187.
 87. Senarathna J, Rege A, Li N, Thakor NV. Laser Speckle Contrast Imaging: theory, instrumentation and applications. *IEEE Rev. Biomed. Eng.* **2013**, *6*, 99–110. doi:10.1109/RBME.2013.2243140.
 88. Kell DB, Zhao H, Pretorius E. Assessment of the impacts of fibrinoid microclots on the microcirculation and endothelial function, using laser speckle and laser Doppler imaging. *Preprints* **2025**, 2025062239. doi:10.20944/preprints202506.2239.v1.
 89. Herrick AL, Murray A. The role of capillaroscopy and thermography in the assessment and management of Raynaud's phenomenon. *Autoimmun. Rev.* **2018**, *17*, 465–472. doi:10.1016/j.autrev.2017.11.036.

90. Wilkinson JD, Leggett SA, Marjanovic EJ, Moore TL, Allen J, Anderson ME, et al. A Multicenter Study of the Validity and Reliability of Responses to Hand Cold Challenge as Measured by Laser Speckle Contrast Imaging and Thermography: Outcome Measures for Systemic Sclerosis-Related Raynaud's Phenomenon. *Arthritis Rheumatol.* **2018**, *70*, 903–911. doi:10.1002/art.40457.
91. Kell DB, Pretorius E. On the utility of nailfold capillaroscopy in detecting the effects of fibrinolytic microclots in diseases involving blood stasis. *Preprints* **2025**, 202505.202356/v202501. doi:10.20944/preprints202505.2356.v1.
92. Cutolo M, Smith V. State of the art on nailfold capillaroscopy: a reliable diagnostic tool and putative biomarker in rheumatology? *Rheumatology* **2013**, *52*, 1933–1940. doi:10.1093/rheumatology/ket153.
93. El Miedany Y, Ismail S, Wadie M, Hassan M. Nailfold capillaroscopy: tips and challenges. *Clin. Rheumatol.* **2022**, *41*, 3629–3640. doi:10.1007/s10067-022-06354-1.
94. Grover C, Jakhar D, Mishra A, Singal A. Nail-fold capillaroscopy for the dermatologists. *Indian. J. Dermatol. Venereol. Leprol.* **2022**, *88*, 300–312. doi:10.25259/IJDVL_514_20.
95. Karbalaie A, Emrani Z, Fatemi A, Etehadavakol M, Erlandsson BE. Practical issues in assessing nailfold capillaroscopic images: A summary. *Clin. Rheumatol.* **2019**, *38*, 2343–2354. doi:10.1007/s10067-019-04644-9.
96. Rodriguez-Reyna TS, Bertolazzi C, Vargas-Guerrero A, Gutiérrez M, Hernández-Molina G, Audisio M, et al. Can nailfold videocapillaroscopy images be interpreted reliably by different observers? Results of an inter-reader and intra-reader exercise among rheumatologists with different experience in this field. *Clin. Rheumatol.* **2019**, *38*, 205–210. doi:10.1007/s10067-018-4041-2.
97. Gracia Tello BDC, SáezComet L, Lledó G, Freire Dapena M, Mesa MA, Martín-Cascón M, et al. Capi-score: a quantitative algorithm for identifying disease patterns in nailfold videocapillaroscopy. *Rheumatology* **2024**, *63*, 3315–3321. doi:10.1093/rheumatology/keae197.
98. Emrani Z, Karbalaie A, Fatemi A, Etehadavakol M, Erlandsson BE. Capillary density: An important parameter in nailfold capillaroscopy. *Microvasc. Res.* **2017**, *109*, 7–18. doi:10.1016/j.mvr.2016.09.001.
99. Karbalaie A, Abtahi F, Fatemi A, Etehadavakol M, Emrani Z, Erlandsson BE. Elliptical broken line method for calculating capillary density in nailfold capillaroscopy: Proposal and evaluation. *Microvasc. Res.* **2017**, *113*, 1–8. doi:10.1016/j.mvr.2017.04.002.
100. Kintrop S, Listkiewicz L, Arnemann PH, Wagner NM. Nailfold videocapillaroscopy—A novel method for the assessment of hemodynamic incoherence on the ICU. *Crit. Care* **2024**, *28*, 400. doi:10.1186/s13054-024-05194-6.
101. El Miedany Y, Ismail S, Wadie Fawzy M, Muller-Ladner U, Giacomelli R, Liakouli V, et al. Towards a consensus on the clinical applications and interpretations of the nailfold capillaroscopy standards in clinical practice: An initiative by the Egyptian Society of Microcirculation. *Arch. Rheumatol.* **2023**, *38*, 451–460. doi:10.46497/ArchRheumatol.2023.9875.
102. El Miedany Y, Ismail S, Wadie M, Muller-Ladner U, Giacomelli R, Liakouli V, et al. Development of a core domain set for nailfold capillaroscopy reporting. *Reumatol. Clin.* **2024**, *20*, 345–352. doi:10.1016/j.reumae.2024.07.003.
103. Etehad Tavakol M, Fatemi A, Karbalaie A, Emrani Z, Erlandsson BE. Nailfold Capillaroscopy in Rheumatic Diseases: Which Parameters Should Be Evaluated? *Biomed. Res. Int.* **2015**, *2015*, 974530. doi:10.1155/2015/974530.
104. Bertolazzi C, Cutolo M, Smith V, Gutierrez M. State of the art on nailfold capillaroscopy in dermatomyositis and polymyositis. *Semin. Arthritis Rheum.* **2017**, *47*, 432–444. doi:10.1016/j.semarthrit.2017.06.001.
105. Cutolo M, Melsens K, Wijnant S, Ingegnoli F, Thevissen K, De Keyser F, et al. Nailfold capillaroscopy in systemic lupus erythematosus: A systematic review and critical appraisal. *Autoimmun. Rev.* **2018**, *17*, 344–352. doi:10.1016/j.autrev.2017.11.025.
106. Smith V, Herrick AL, Ingegnoli F, Damjanov N, De Angelis R, Denton CP, et al. Standardisation of nailfold capillaroscopy for the assessment of patients with Raynaud's phenomenon and systemic sclerosis. *Autoimmun. Rev.* **2020**, *19*, 102458. doi:10.1016/j.autrev.2020.102458.
107. Smith V, Ickinger C, Hysa E, Snow M, Frech T, Sulli A, et al. Nailfold capillaroscopy. *Best. Pract. Res. Clin. Rheumatol.* **2023**, *37*, 101849. doi:10.1016/j.berh.2023.101849.
108. Patil A, Sood I. Nailfold Capillaroscopy in Rheumatic Diseases. *Intech Open* **2020**, 72602. doi:10.5772/intechopen.92786.
109. Ocampo-Garza SS, Villarreal-Alarcon MA, Villarreal-Trevino AV, Ocampo-Candiani J. Capillaroscopy: A Valuable Diagnostic Tool. *Actas. Dermosifiliogr.* **2019**, *110*, 347–352. doi:10.1016/j.ad.2018.10.018.
110. Dundar HA, Adrovic A, Demir S, Demir F, Cakmak F, Ayaz NA, et al. Description of the characteristics of the nailfold capillary structure in healthy children: a multi-centric study. *Rheumatology* **2024**, *63*, SI152–SI159. doi:10.1093/rheumatology/keae296.
111. Altörök N, Wang Y, Kahaleh B. Endothelial dysfunction in systemic sclerosis. *Curr. Opin. Rheumatol.* **2014**, *26*, 615–620. doi:10.1097/BOR.0000000000000112.
112. Matucci-Cerinic M, Kahaleh B, Wigley FM. Review: evidence that systemic sclerosis is a vascular disease. *Arthritis Rheum.* **2013**, *65*, 1953–1962. doi:10.1002/art.37988.
113. Moschetti L, Piantoni S, Vizzardi E, Sciatti E, Riccardi M, Franceschini F, et al. Endothelial Dysfunction in Systemic Lupus Erythematosus and Systemic Sclerosis: A Common Trigger for Different Microvascular Diseases. *Front. Med.* **2022**, *9*, 849086. doi:10.3389/fmed.2022.849086.

114. Mostmans Y, Cutolo M, Giddelo C, Decuman S, Melsens K, Declercq H, et al. The role of endothelial cells in the vasculopathy of systemic sclerosis: A systematic review. *Autoimmun. Rev.* **2017**, *16*, 774–786. doi:10.1016/j.autrev.2017.05.024.
115. Ota Y, Kuwana M. Endothelial cells and endothelial progenitor cells in the pathogenesis of systemic sclerosis. *Eur. J. Rheumatol.* **2020**, *7*, S139–S146. doi:10.5152/eurjrheum.2019.19158.
116. Patnaik E, Lyons M, Tran K, Pattanaik D. Endothelial Dysfunction in Systemic Sclerosis. *Int. J. Mol. Sci.* **2023**, *24*, 14385. doi:10.3390/ijms241814385.
117. Silva I, Teixeira A, Oliveira J, Almeida I, Almeida R, Aguas A, et al. Endothelial dysfunction and nailfold videocapillaroscopy pattern as predictors of digital ulcers in systemic sclerosis: a cohort study and review of the literature. *Clin. Rev. Allergy Immunol.* **2015**, *49*, 240–252. doi:10.1007/s12016-015-8500-0.
118. Matucci-Cerinic M, Hughes M, Taliani G, Kahaleh B. Similarities between COVID-19 and systemic sclerosis early vasculopathy: A “viral” challenge for future research in scleroderma. *Autoimmun. Rev.* **2021**, *20*, 102899. doi:10.1016/j.autrev.2021.102899.
119. Kuchler T, Gunthner R, Ribeiro A, Hausinger R, Streese L, Wohln A, et al. Persistent endothelial dysfunction in post-COVID-19 syndrome and its associations with symptom severity and chronic inflammation. *Angiogenesis* **2023**, *26*, 547–563. doi:10.1007/s10456-023-09885-6.
120. Santoro L, Zaccone V, Falsetti L, Ruggieri V, Danese M, Miro C, et al. Role of Endothelium in Cardiovascular Sequelae of Long COVID. *Biomedicines* **2023**, *11*, 2239. doi:10.3390/biomedicines11082239.
121. Xu SW, Ilyas I, Weng JP. Endothelial dysfunction in COVID-19: An overview of evidence, biomarkers, mechanisms and potential therapies. *Acta Pharmacol. Sin.* **2023**, *44*, 695–709. doi:10.1038/s41401-022-00998-0.
122. Aljadah M, Khan N, Beyer AM, Chen Y, Blanker A, Widlansky ME. Clinical Implications of COVID-19-Related Endothelial Dysfunction. *JACC Adv.* **2024**, *3*, 101070. doi:10.1016/j.jacadv.2024.101070.
123. Perico L, Benigni A, Remuzzi G. SARS-CoV-2 and the spike protein in endotheliopathy. *Trends Microbiol.* **2024**, *32*, 53–67. doi:10.1016/j.tim.2023.06.004.
124. Wu X, Xiang M, Jing H, Wang C, Novakovic VA, Shi J. Damage to endothelial barriers and its contribution to long COVID. *Angiogenesis* **2024**, *27*, 5–22. doi:10.1007/s10456-023-09878-5.
125. Kruger A, Joffe D, Lloyd-Jones G, Khan MA, Šalamon Š, Laubscher GJ, et al. Vascular pathogenesis in acute and long covid: current insights and therapeutic outlook. *Semin. Throm. Hemost.* **2025**, *51*, 256–271. doi:10.1055/s-0044-1790603.
126. Çakmak F, Demirbuga A, Demirkol D, Gümüş S, Torun SH, Kayaalp GK, et al. Nailfold capillaroscopy: A sensitive method for evaluating microvascular involvement in children with SARS-CoV-2 infection. *Microvasc. Res.* **2021**, *138*, 104196. doi:10.1016/j.mvr.2021.104196.
127. Jud P, Gressenberger P, Muster V, Avian A, Meinitzer A, Strohmaier H, et al. Evaluation of Endothelial Dysfunction and Inflammatory Vasculopathy After SARS-CoV-2 Infection-A Cross-Sectional Study. *Front. Cardiovasc. Med.* **2021**, *8*, 750887. doi:10.3389/fcvm.2021.750887.
128. Natalello G, De Luca G, Gigante L, Campochiaro C, De Lorenzis E, Verardi L, et al. Nailfold capillaroscopy findings in patients with coronavirus disease 2019: Broadening the spectrum of COVID-19 microvascular involvement. *Microvasc. Res.* **2021**, *133*, 104071. doi:10.1016/j.mvr.2020.104071.
129. Wollina U, Kanitakis J, Baran R. Nails and COVID-19—A comprehensive review of clinical findings and treatment. *Dermatol. Ther.* **2021**, *34*, e15100. doi:10.1111/dth.15100.
130. Armağan B, Özdemir B, Aypak A, Akıncı E, Karakaş Ö, Güven SC, et al. Evaluation of Coronavirus Disease-2019 Patients with Nailfold Capillaroscopy. *Namik Kemal Med. J.* **2022**, *10*, 80–86. doi:10.4274/nkmj.galenos.2021.97269.
131. Mostmans Y, Smith V, Cutolo M, Melsens K, Battist S, Benslimane A, et al. Nailfold videocapillaroscopy and serum vascular endothelial growth factor in probable COVID-19-induced chilblains: a cross-sectional study to assess microvascular impairment. *Br. J. Dermatol.* **2022**, *187*, 1017–1019. doi:10.1111/bjd.21785.
132. Rosei CA, Gaggero A, Fama F, Malerba P, Chiarini G, Nardin M, et al. Skin capillary alterations in patients with acute SarsCoV2 infection. *J. Hypertens.* **2022**, *40*, 2385–2393. doi:10.1097/HJH.0000000000003271.
133. Sulli A, Gotelli E, Bica PF, Schiavetti I, Pizzorni C, Aloe T, et al. Detailed videocapillaroscopic microvascular changes detectable in adult COVID-19 survivors. *Microvasc. Res.* **2022**, *142*, 104361. doi:10.1016/j.mvr.2022.104361.
134. Cutolo M, Sulli A, Smith V, Gotelli E. Emerging nailfold capillaroscopic patterns in COVID-19: From acute patients to survivors. *Reumatismo* **2023**, *74*, 139–143. doi:10.4081/reumatismo.2022.1555.
135. Mondini L, Confalonieri P, Pozzan R, Ruggero L, Trotta L, Lerda S, et al. Microvascular Alteration in COVID-19 Documented by Nailfold Capillaroscopy. *Diagnostics* **2023**, *13*, 1905. doi:10.3390/diagnostics13111905.
136. Kaplan H, Cengiz G, Şaş S, Kara H. Comparison of nailfold capillaroscopy findings in COVID-19 survivors with and without rheumatic disease: a case-control study. *Cucurova Med. J.* **2024**, *49*, 71–80. doi:10.17826/cumj.1382804.
137. Kastarli Bakay OS, Cetin N, Bakay U, Cinar G, Goksin S. A Window into the Vascular Endothelium in COVID-19: Nails. *Dermatol. Pract. Concept.* **2025**, *15*, 4927. doi:10.5826/dpc.1501a4927.
138. Wilkinson S, Wilkinson J, Grace A, Lyon D, Mellor M, Yunus T, et al. Imaging the microvasculature using nailfold capillaroscopy in patients with coronavirus disease-2019; A cross-sectional study. *Microvasc. Res.* **2025**, *159*, 104796.

- doi:10.1016/j.mvr.2025.104796.
139. Bunch CM, Moore EE, Moore HB, Neal MD, Thomas AV, Zackariya N, et al. Immuno-thrombotic Complications of COVID-19: Implications for Timing of Surgery and Anticoagulation. *Front. Surg.* **2022**, *9*, 889999. doi:10.3389/fsurg.2022.889999.
 140. Grobbelaar LM, Venter C, Vlok M, Ngoepe M, Laubscher GJ, Lourens PJ, et al. SARS-CoV-2 spike protein S1 induces fibrin(ogen) resistant to fibrinolysis: implications for microclot formation in COVID-19. *Biosci. Rep.* **2021**, *41*, BSR20210611. doi:10.1042/BSR20210611.
 141. Grobbelaar LM, Kruger A, Venter C, Burger EM, Laubscher GJ, Maponga TG, et al. Relative hypercoagulopathy of the SARS-CoV-2 Beta and Delta variants when compared to the less severe Omicron variants is related to TEG parameters, the extent of fibrin amyloid microclots, and the severity of clinical illness. *Semin. Thromb. Haemost.* **2022**, *48*, 858–868. doi:10.1055/s-0042-1756306.
 142. Grobler C, Maphumulo SC, Grobbelaar LM, Bredenkamp J, Laubscher J, Lourens PJ, et al. COVID-19: The Rollercoaster of Fibrin(ogen), D-dimer, von Willebrand Factor, P-selectin and Their Interactions with Endothelial Cells, Platelets and Erythrocytes. *Int. J. Mol. Sci.* **2020**, *21*, 5168. doi:10.3390/ijms21145168.
 143. Cousins CC, Alosco ML, Cousins HC, Chua A, Steinberg EG, Chapman KR, et al. Nailfold Capillary Morphology in Alzheimer's Disease Dementia. *J. Alzheimers. Dis.* **2018**, *66*, 601–611. doi:10.3233/JAD-180658.
 144. Ciaffi J, Ajasllari N, Mancarella L, Brusi V, Meliconi R, Ursini F. Nailfold capillaroscopy in common non-rheumatic conditions: A systematic review and applications for clinical practice. *Microvasc. Res.* **2020**, *131*, 104036. doi:10.1016/j.mvr.2020.104036.
 145. Grobler C, van Tongeren M, Gettemans J, Kell D, Pretorius E. Alzheimer-type dementia: a systems view Provides a unifying explanation of its development. *J. Alzheimer's Dis.* **2023**, *91*, 43–70. doi:10.3233/JAD-220720.
 146. Pretorius L, Kell DB, Pretorius E. Iron Dysregulation and Dormant Microbes as Causative Agents for Impaired Blood Rheology and Pathological Clotting in Alzheimer's Type Dementia. *Front. Neurosci.* **2018**, *12*, 851. doi:10.3389/fnins.2018.00851.
 147. Deshayes S, Auboire L, Jaussaud R, Lidove O, Parienti JJ, Triclin N, et al. Prevalence of Raynaud phenomenon and nailfold capillaroscopic abnormalities in Fabry disease: A cross-sectional study. *Medicine* **2015**, *94*, e780. doi:10.1097/MD.0000000000000780.
 148. Faro DC, Di Pino FL, Monte IP. Inflammation, Oxidative Stress, and Endothelial Dysfunction in the Pathogenesis of Vascular Damage: Unraveling Novel Cardiovascular Risk Factors in Fabry Disease. *Int. J. Mol. Sci.* **2024**, *25*, 8273. doi:10.3390/ijms25158273.
 149. Faro DC, Di Pino FL, Rodolico MS, Costanzo L, Losi V, Di Pino L, et al. Relationship between Capillaroscopic Architectural Patterns and Different Variant Subgroups in Fabry Disease: Analysis of Cases from a Multidisciplinary Center. *Genes* **2024**, *15*, 1101. doi:10.3390/genes15081101.
 150. Wasik JS, Simon RW, Meier T, Steinmann B, Amann-Vesti BR. Nailfold capillaroscopy: Specific features in Fabry disease. *Clin. Hemorheol. Microcirc.* **2009**, *42*, 99–106. doi:10.3233/CH-2009-1158.
 151. De Martinis M, Sirufo MM, Ginaldi L. Raynaud's phenomenon and nailfold capillaroscopic findings in anorexia nervosa. *Curr. Med. Res. Opin.* **2018**, *34*, 547–550. doi:10.1080/03007995.2017.1417828.
 152. Sirufo MM, Ginaldi L, De Martinis M. Peripheral Vascular Abnormalities in Anorexia Nervosa: A Psycho-Neuro-Immune-Metabolic Connection. *Int. J. Mol. Sci.* **2021**, *22*, 5043. doi:10.3390/ijms22095043.
 153. Matsuda S, Kotani T, Wakura R, Suzuka T, Kuwabara H, Kiboshi T, et al. Examination of nailfold videocapillaroscopy findings in ANCA-associated vasculitis. *Rheumatology* **2023**, *62*, 747–757. doi:10.1093/rheumatology/keac402.
 154. Triggianese P, D'Antonio A, Nesi C, Kroegler B, Di Marino M, Conigliaro P, et al. Subclinical microvascular changes in ANCA-vasculitides: The role of optical coherence tomography angiography and nailfold capillaroscopy in the detection of disease-related damage. *Orphanet J. Rare Dis.* **2023**, *18*, 184. doi:10.1186/s13023-023-02782-7.
 155. Screm G, Mondini L, Confalonieri P, Salton F, Trotta L, Barbieri M, et al. Nailfold Capillaroscopy Analysis Can Add a New Perspective to Biomarker Research in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. *Diagnostics* **2024**, *14*, 254. doi:10.3390/diagnostics14030254.
 156. Sullivan MM, Abril A, Aslam N, Ball CT, Berianu F. Nailfold videocapillaroscopy in antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Res. Ther.* **2024**, *26*, 4. doi:10.1186/s13075-023-03227-z.
 157. Arslan Uku S, Demir B, Cicek D, Inan Yuksel E. Assessment of nail findings in children with atopic dermatitis. *Clin. Exp. Dermatol.* **2021**, *46*, 1511–1517. doi:10.1111/ced.14783.
 158. Aytekin S, Yuksel EP, Aydin F, Senturk N, Ozden MG, Canturk T, et al. Nailfold capillaroscopy in Behçet disease, performed using videodermoscopy. *Clin. Exp. Dermatol.* **2014**, *39*, 443–447. doi:10.1111/ced.12343.
 159. Mercadé-Torras JM, Guillén-Del-Castillo A, Buján S, Solans-Laqué R. Nailfold videocapillaroscopy abnormalities and vascular manifestations in Behçet's syndrome. *Clin. Exp. Rheumatol.* **2024**, *42*, 2065–2070. doi:10.55563/clinexprheumatol/v5mz8d.
 160. Monoe K, Takahashi A, Abe K, Kanno Y, Watanabe H, Ohira H. Evaluation of nail fold capillaroscopy findings in patients with primary biliary cirrhosis. *Hepatol. Res.* **2014**, *44*, E129–E136. doi:10.1111/hepr.12255.

161. Kim M. Nail fold capillaroscopy as a potential tool to evaluate breast tumor. *J. Anal. Sci. Technol.* **2024**, *15*, 35. doi:10.1186/s40543-024-00449-x.
162. Screm G, Mondini L, Salton F, Confalonieri P, Trotta L, Barbieri M, et al. Vascular Endothelial Damage in COPD: Where Are We Now, Where Will We Go? *Diagnostics* **2024**, *14*, 950. doi:10.3390/diagnostics14090950.
163. Corrado A, Carpagnano GE, Gaudio A, Foschino-Barbaro MP, Cantatore FP. Nailfold capillaroscopic findings in systemic sclerosis related lung fibrosis and in idiopathic lung fibrosis. *Jt. Bone Spine* **2010**, *77*, 570–574. doi:10.1016/j.jbspin.2010.02.019.
164. Yuksel EP, Yuksel S, Soylu K, Aydin F. Microvascular abnormalities in asymptomatic chronic smokers: A videocapillaroscopic study. *Microvasc. Res.* **2019**, *124*, 51–53. doi:10.1016/j.mvr.2019.03.004.
165. Mostmans Y, Maurer M, Richert B, Smith V, Melsens K, De Maertelaer V, et al. Chronic spontaneous urticaria: Evidence of systemic microcirculatory changes. *Clin. Transl. Allergy* **2024**, *14*, e12335. doi:10.1002/clt2.12335.
166. Bernardino V, Rodrigues A, Lladó A, Panarra A. Nailfold capillaroscopy and autoimmune connective tissue diseases in patients from a Portuguese nailfold capillaroscopy clinic. *Rheumatol. Int.* **2020**, *40*, 295–301. doi:10.1007/s00296-019-04427-0.
167. Munteanu A, Kundnani NR, Caraba A. Nailfold capillaroscopy abnormalities and pulmonary hypertension in mixed connective tissue disease and systemic sclerosis patients. *Eur. Rev. Med. Pharmacol. Sci.* **2024**, *28*, 1314–1326. doi:10.26355/eurrev_202402_35453.
168. Tang Z, Yang F, Wu H, Zhao Y, Shen J, Hong H, et al. Alterations in nailfold videocapillaroscopy among patients with connective tissue diseases combined with pulmonary arterial hypertension: A cross-sectional study. *Sci. Rep.* **2025**, *15*, 8647. doi:10.1038/s41598-025-92093-7.
169. Maslianitsyna A, Ermolinskiy P, Lugovtsov A, Pigurenko A, Sasonko M, Gurfinkel Y, et al. Multimodal Diagnostics of Microrheologic Alterations in Blood of Coronary Heart Disease and Diabetic Patients. *Diagnostics* **2021**, *11*, 76. doi:10.3390/diagnostics11010076.
170. Manfredi A, Sebastiani M, Cassone G, Pipitone N, Giuggioli D, Colaci M, et al. Nailfold capillaroscopic changes in dermatomyositis and polymyositis. *Clin. Rheumatol.* **2015**, *34*, 279–284. doi:10.1007/s10067-014-2795-8.
171. McBride JD, Sontheimer RD. Proximal nailfold microhemorrhage events are manifested as distal cuticular (eponychial) hemosiderin-containing deposits (CEHD) (syn. Maricq sign) and can aid in the diagnosis of dermatomyositis and systemic sclerosis. *Dermatol. Online J.* **2016**, *22*, 13030.
172. Cutolo M, Smith V. Detection of microvascular changes in systemic sclerosis and other rheumatic diseases. *Nat. Rev. Rheumatol.* **2021**, *17*, 665–677. doi:10.1038/s41584-021-00685-0.
173. Monfort JB, Chasset F, Barbaud A, Frances C, Senet P. Nailfold capillaroscopy findings in cutaneous lupus erythematosus patients with or without digital lesions and comparison with dermatomyositis patients: A prospective study. *Lupus* **2021**, *30*, 1207–1213. doi:10.1177/09612033211010329.
174. Pachman LM, Morgan G, Klein-Gitelman MS, Ahsan N, Khojah A. Nailfold capillary density in 140 untreated children with juvenile dermatomyositis: an indicator of disease activity. *Pediatr. Rheumatol. Online J.* **2023**, *21*, 118. doi:10.1186/s12969-023-00903-x.
175. Flatley EM, Collins D, Lukowiak TM, Miller JH. Nailfold microscopy in adult-onset dermatomyositis in association with myositis antibodies. *Arch. Dermatol. Res.* **2024**, *317*, 34. doi:10.1007/s00403-024-03521-z.
176. Trevisan G, Bonin S, Tucci S, Bilancini S. Dermatomyositis: Nailfold capillaroscopy patterns and a general survey. *Acta Dermatovenereol. Alp. Pannonica Adriat.* **2024**, *33*, 69–79.
177. Xu H, Qian J. The role of nailfold video-capillaroscopy in the assessment of dermatomyositis. *Rheumatology* **2025**, *64*, 2987–2994. doi:10.1093/rheumatology/keae677.
178. Yılmaz Tuğan B, Sönmez HE, Güngör M, Yüksel N, Karabaş L. Preclinical ocular microvascular changes in juvenile dermatomyositis: A pilot optical coherence tomography angiography study. *Microvasc. Res.* **2022**, *143*, 104382. doi:10.1016/j.mvr.2022.104382.
179. Piette Y, Reynaert V, Vanhaecke A, Bonroy C, Gutermuth J, Sulli A, et al. Standardised interpretation of capillaroscopy in autoimmune idiopathic inflammatory myopathies: A structured review on behalf of the EULAR study group on microcirculation in Rheumatic Diseases. *Autoimmun. Rev.* **2022**, *21*, 103087. doi:10.1016/j.autrev.2022.103087.
180. Abdelmaksoud AA, Daifallah SM, Salah NY, Saber AS. Nail fold microangiopathy in adolescents with type 1 diabetes: Relation to diabetic vascular complications. *Microcirculation* **2022**, *29*, e12771. doi:10.1111/micc.12771.
181. Kaminska-Winciorek G, Deja G, Polańska J, Jarosz-Chobot P. Diabetic microangiopathy in capillaroscopic examination of juveniles with diabetes type 1. *Adv. Hyg. Exp. Med./Postepy Higieny i Medycyny Doswiadczalnej* **2012**, *66*, 51–59.
182. Shah R, Petch J, Nelson W, Roth K, Noseworthy MD, Ghassemi M, et al. Nailfold capillaroscopy and deep learning in diabetes. *J. Diabetes* **2023**, *15*, 145–151. doi:10.1111/1753-0407.13354.
183. Abd El-Khalik DM, Hafez EA, Hassan HE, Mahmoud AE, Ashour DM, Morshedy NA. Nail Folds Capillaries Abnormalities Associated With Type 2 Diabetes Mellitus Progression and Correlation with Diabetic Retinopathy. *Clin. Med. Insights Endocrinol. Diabetes* **2022**, *15*, 11795514221122828. doi:10.1177/11795514221122828.
184. Ahmad S, Pai VV, Sharath A, Ghodge R, Shukla P. Qualitative analysis of nailfold capillaries in diabetes and diabetic

- retinopathy using dermatoscope in patients with coloured skin. *Indian J. Dermatol. Venereol Leprol* **2024**, *90*, 139–149. doi:10.25259/IJDVL_710_2022.
185. Maldonado G, Guerrero R, Paredes C, Rios C. Nailfold capillaroscopy in diabetes mellitus. *Microvasc. Res.* **2017**, *112*, 41–46. doi:10.1016/j.mvr.2017.03.001.
 186. Pretorius E, Oberholzer HM, van der Spuy WJ, Swanepoel AC, Soma P. Qualitative scanning electron microscopy analysis of fibrin networks and platelet abnormalities in diabetes. *Blood Coagul. Fibrinol* **2011**, *22*, 463–467. doi:10.1097/MBC.0b013e3283468a0d.
 187. Pretorius E, Bester J, Vermeulen N, Alummoottil S, Soma P, Buys AV, et al. Poorly controlled type 2 diabetes is accompanied by significant morphological and ultrastructural changes in both erythrocytes and in thrombin-generated fibrin: implications for diagnostics. *Cardiovasc. Diabetol.* **2015**, *134*, 30. doi:10.1186/s12933-015-0192-5.
 188. Pazos-Moura CC, Moura EG, Bouskela E, Torres Filho IP, Breitenbach MM. Nailfold capillaroscopy in non-insulin dependent diabetes mellitus: blood flow velocity during rest and post-occlusive reactive hyperaemia. *Clin. Physiol.* **1990**, *10*, 451–461. doi:10.1111/j.1475-097x.1990.tb00825.x.
 189. Maldonado G, Chacko A, Lichtenberg R, Ionescu M, Rios C. Nailfold capillaroscopy in diabetes mellitus: A case of neo-angiogenesis after achieving normoglycemia. *Oxf. Med. Case Rep.* **2022**, *2022*, omac088. doi:10.1093/omcr/omac088.
 190. Lisco G, Triggiani V. Computerized nailfold video-capillaroscopy in type 2 diabetes: A cross-sectional study on 102 outpatients. *J. Diabetes* **2023**, *15*, 890–899. doi:10.1111/1753-0407.13442.
 191. Elumalai S, Krishnamoorthi N, Periyasamy N, Farazullah M, Raj K, Mahadevan S. Analysis of microvascular pattern in diabetes mellitus condition using the nailfold capillaroscopy images. *Proc. Inst. Mech. Eng. H* **2024**, *238*, 340–347. doi:10.1177/09544119231224510.
 192. Bakirci S, Celik E, Acikgoz SB, Erturk Z, Tocoglu AG, Imga NN, et al. The evaluation of nailfold videocapillaroscopy findings in patients with type 2 diabetes with and without diabetic retinopathy. *North. Clin. Istanb.* **2019**, *6*, 146–150. doi:10.14744/nci.2018.02222.
 193. Uyar S, Balkarli A, Erol MK, Yeşil B, Tokuç A, Durmaz D, et al. Assessment of the Relationship between Diabetic Retinopathy and Nailfold Capillaries in Type 2 Diabetics with a Noninvasive Method: Nailfold Videocapillaroscopy. *J. Diabetes Res.* **2016**, *2016*, 7592402. doi:10.1155/2016/7592402.
 194. Chao CYL, Zheng YP, Cheing GLY. The association between skin blood flow and edema on epidermal thickness in the diabetic foot. *Diabetes Technol. Ther.* **2012**, *14*, 602–609. doi:10.1089/dia.2011.0301.
 195. Yilmaz U, Ayan A, Uyar S, Inci A, Ozer H, Yilmaz FT, et al. Capillaroscopic appearance of nailfold vasculature of diabetic nephropathy patients. *Arch. Endocrinol. Metab.* **2022**, *66*, 295–302. doi:10.20945/2359-3997000000475.
 196. Hsu PC, Liao PY, Huang SW, Chang HH, Chiang JY, Lo LC. Nailfold capillary abnormalities as indicators of diabetic nephropathy progression: a cross-sectional study in type 2 diabetes. *Ann. Med.* **2025**, *57*, 2458766. doi:10.1080/07853890.2025.2458766.
 197. Haak ES, Usadel KH, Kohleisen M, Yilmaz A, Kusterer K, Haak T. The effect of alpha-lipoic acid on the neurovascular reflex arc in patients with diabetic neuropathy assessed by capillary microscopy. *Microvasc. Res.* **1999**, *58*, 28–34. doi:10.1006/mvre.1999.2151.
 198. Gou H, Liu J. Non-ocular biomarkers for early diagnosis of diabetic retinopathy by non-invasive methods. *Front. Endocrinol.* **2025**, *16*, 1496851. doi:10.3389/fendo.2025.1496851.
 199. Mahajan M, Kaur T, Singh K, Mahajan BB. Evaluation of nail fold capillaroscopy changes in patients with diabetic retinopathy and healthy controls, and its correlation with disease duration, HbA1c levels and severity of diabetic retinopathy: An observational study. *Indian. J. Dermatol. Venereol. Leprol.* **2024**, *90*, 782–788. doi:10.25259/IJDVL_232_2023.
 200. Okabe T, Kunikata H, Yasuda M, Kodama S, Maeda Y, Nakano J, et al. Relationship between nailfold capillaroscopy parameters and the severity of diabetic retinopathy. *Graefes Arch. Clin. Exp. Ophthalmol.* **2024**, *262*, 759–768. doi:10.1007/s00417-023-06220-z.
 201. Shikama M, Sonoda N, Morimoto A, Suga S, Tajima T, Kozawa J, et al. Association of crossing capillaries in the finger nailfold with diabetic retinopathy in type 2 diabetes mellitus. *J. Diabetes Investig.* **2021**, *12*, 1007–1014. doi:10.1111/jdi.13444.
 202. Hughes M, Herrick AL. Digital ulcers in systemic sclerosis. *Rheumatology* **2017**, *56*, 14–25. doi:10.1093/rheumatology/kew047.
 203. Hughes M, Allanore Y, Chung L, Pauling JD, Denton CP, Matucci-Cerinic M. Raynaud phenomenon and digital ulcers in systemic sclerosis. *Nat. Rev. Rheumatol.* **2020**, *16*, 208–221. doi:10.1038/s41584-020-0386-4.
 204. Herrick AL. Raynaud's phenomenon and digital ulcers: advances in evaluation and management. *Curr. Opin. Rheumatol.* **2021**, *33*, 453–462. doi:10.1097/BOR.0000000000000826.
 205. Apte Sengun O, Ergun T, Guctekin T, Alibaz Oner F. Endothelial dysfunction, thrombophilia, and nailfold capillaroscopic features in livedoid vasculopathy. *Microvasc. Res.* **2023**, *150*, 104591. doi:10.1016/j.mvr.2023.104591.
 206. Angeloudi E, Bekiari E, Pagkopoulou E, Anyfanti P, Doumas M, Garyfallos A, et al. Study of Peripheral Microcirculation Assessed by Nailfold Video-Capillaroscopy and Association with Markers of Endothelial Dysfunction and Inflammation in Rheumatoid Arthritis. *Mediterr. J. Rheumatol.* **2022**, *33*, 375–379. doi:10.31138/mjr.33.3.375.

207. Frödin T, Bengtsson A, Skogh M. Nail fold capillaroscopy findings in patients with primary fibromyalgia. *Clin. Rheumatol.* **1988**, *7*, 384–388. doi:10.1007/BF02239197.
208. Bennett RM, Clark SR, Campbell SM, Ingram SB, Burckhardt CS, Nelson DL, et al. Symptoms of Raynaud's syndrome in patients with fibromyalgia. A study utilizing the Nielsen test, digital photoplethysmography, and measurements of platelet alpha 2-adrenergic receptors. *Arthritis Rheum.* **1991**, *34*, 264–269. doi:10.1002/art.1780340303.
209. Scolnik M, Vasta B, Hart DJ, Shipley JA, McHugh NJ, Pauling JD. Symptoms of Raynaud's phenomenon (RP) in fibromyalgia syndrome are similar to those reported in primary RP despite differences in objective assessment of digital microvascular function and morphology. *Rheumatol. Int.* **2016**, *36*, 1371–1377. doi:10.1007/s00296-016-3483-6.
210. Esen E, Çetin A. Microvascular functions in patients with fibromyalgia syndrome: effects of physical exercise. *Turk. J. Phys. Med. Rehabil.* **2017**, *63*, 215–223. doi:10.5606/tftrd.2017.351.
211. Choi DH, Kim HS. Quantitative analysis of nailfold capillary morphology in patients with fibromyalgia. *Korean J. Intern. Med.* **2015**, *30*, 531–537. doi:10.3904/kjim.2015.30.4.531.
212. Appelman B, Charlton BT, Goulding RP, Kerkhoff TJ, Breedveld EA, Noort W, et al. Muscle abnormalities worsen after post-exertional malaise in long COVID. *Nat. Commun.* **2024**, *15*, 17. doi:10.1038/s41467-023-44432-3.
213. Coşkun Benlidayı I, Kayacan Erdoğan E, Sarıyıldız A. The evaluation of nailfold capillaroscopy pattern in patients with fibromyalgia. *Arch. Rheumatol.* **2021**, *36*, 341–348. doi:10.46497/ArchRheumatol.2021.8359.
214. Salah NY. Vascular endothelial growth factor (VEGF), tissue inhibitors of metalloproteinase-1 (TIMP-1) and nail fold capillaroscopy changes in children and adolescents with Gaucher disease; relation to residual disease severity. *Cytokine* **2020**, *133*, 155120. doi:10.1016/j.cyto.2020.155120.
215. Dima A, Berza I, Popescu DN, Parvu MI. Nailfold capillaroscopy in systemic diseases: short overview for internal medicine. *Rom. J. Intern. Med.* **2021**, *59*, 201–217. doi:10.2478/rjim-2021-0007.
216. Herrick AL, Berks M, Taylor CJ. Quantitative nailfold capillaroscopy-update and possible next steps. *Rheumatology* **2021**, *60*, 2054–2065. doi:10.1093/rheumatology/keab006.
217. Komai M, Takeno D, Fujii C, Nakano J, Ohsaki Y, Shirakawa H. Nailfold capillaroscopy: A comprehensive review on its usefulness in both clinical diagnosis and improving unhealthy dietary lifestyles. *Nutrients* **2024**, *16*, 1914. doi:10.3390/nu16121914.
218. Mansueto N, Rotondo C, Corrado A, Cantatore FP. Nailfold capillaroscopy : a comprehensive review on common findings and clinical usefulness in non-rheumatic disease. *J. Med. Investig.* **2021**, *68*, 6–14. doi:10.2152/jmi.68.6.
219. Abularrage CJ, Sidawy AN, Aidinian G, Singh N, Weiswasser JM, Arora S. Evaluation of the microcirculation in vascular disease. *J. Vasc. Surg.* **2005**, *42*, 574–581. doi:10.1016/j.jvs.2005.05.019.
220. Cousins CC, Chou JC, Greenstein SH, Brauner SC, Shen LQ, Turalba AV, et al. Resting nailfold capillary blood flow in primary open-angle glaucoma. *Br. J. Ophthalmol.* **2019**, *103*, 203–207. doi:10.1136/bjophthalmol-2018-311846.
221. Yüksel S, Yüksel EP, Meriç M. Abnormal nailfold videocapillaroscopic findings in heart failure patients with preserved ejection fraction. *Clin. Hemorheol. Microcirc.* **2021**, *77*, 115–121. doi:10.3233/CH-200968.
222. Pancar GS, Kaynar T. Nailfold capillaroscopic changes in patients with chronic viral hepatitis. *Microvasc. Res.* **2020**, *129*, 103970. doi:10.1016/j.mvr.2019.103970.
223. Mishra A, Grover C, Singal A, Narang S, Das GK. Nailfold capillary changes in newly diagnosed hypertensive patients: An observational analytical study. *Microvasc. Res.* **2021**, *136*, 104173. doi:10.1016/j.mvr.2021.104173.
224. Kubo S, Todoroki Y, Nakayamada S, Nakano K, Satoh M, Nawata A, et al. Significance of nailfold videocapillaroscopy in patients with idiopathic inflammatory myopathies. *Rheumatology* **2019**, *58*, 120–130. doi:10.1093/rheumatology/key257.
225. Sambataro D, Sambataro G, Libra A, Vignigni G, Pino F, Fagone E, et al. Nailfold Videocapillaroscopy is a Useful Tool to Recognize Definite Forms of Systemic Sclerosis and Idiopathic Inflammatory Myositis in Interstitial Lung Disease Patients. *Diagnostics* **2020**, *10*, 253. doi:10.3390/diagnostics10050253.
226. Mugii N, Hamaguchi Y, Horii M, Fushida N, Ikeda T, Oishi K, et al. Longitudinal changes in nailfold videocapillaroscopy findings differ by myositis-specific autoantibody in idiopathic inflammatory myopathy. *Rheumatology* **2023**, *62*, 1326–1334. doi:10.1093/rheumatology/keac401.
227. Bogojevic M, Markovic Vlasisavljevic M, Medjedovic R, Strujic E, Pravilovic Lutovac D, Pavlov-Dolijanovic S. Nailfold Capillaroscopy Changes in Patients with Idiopathic Inflammatory Myopathies. *J. Clin. Med.* **2024**, *13*, 5550. doi:10.3390/jcm13185550.
228. Sieiro Santos C, Tandaipan JL, Castillo D, Codes H, Martínez-Martínez L, Magallares B, et al. Nailfold videocapillaroscopy findings correlate with lung outcomes in idiopathic inflammatory myopathies-related interstitial lung disease. *Rheumatology* **2024**, *63*, keae669. doi:10.1093/rheumatology/keae669.
229. Gedik B, Erol MK, Bulut M, Dogan B, Bozdogan YC, Ekinci R, et al. Proximal nailfold videocapillaroscopy findings of patients with idiopathic macular telangiectasia type 2. *Indian J. Ophthalmol.* **2024**, *72*, S148–S152. doi:10.4103/IJO.IJO_1731_23.
230. Aggarwal B, Gandhi V, Singal A, Aggarwal A, Saha S. Nail fold capillaroscopy in leprosy: Unveiling the microvascular changes. *Microvasc. Res.* **2024**, *155*, 104712. doi:10.1016/j.mvr.2024.104712.

231. Gotelli E, Campitiello R, Pizzorni C, Sammori S, Aitella E, Ginaldi L, et al. Multicentre retrospective detection of nailfold videocapillaroscopy abnormalities in long covid patients. *RMD Open* **2025**, *11*. doi:10.1136/rmdopen-2025-005469.
232. Kell DB, Khan MA, Pretorius E. Fibrinoid microclots in Long COVID: Assessing the actual evidence properly. *Res. Pract. Thromb. Haemost.* **2024**, *8*, 102566. doi:10.1016/j.rpth.2024.102566.
233. Zhao T, Lin FA, Chen HP. Pattern of Nailfold Capillaroscopy in Patients With Systemic Lupus Erythematosus. *Arch. Rheumatol.* **2020**, *35*, 568–574. doi:10.46497/ArchRheumatol.2020.7763.
234. Bergkamp SC, Schonenberg-Meinema D, Nassar-Sheikh Rashid A, Melsens K, Vanhaecke A, Boumans MJH, et al. Reliable detection of subtypes of nailfold capillary haemorrhages in childhood-onset systemic lupus erythematosus. *Clin. Exp. Rheumatol.* **2021**, *39*, 1126–1131. doi:10.55563/clinexprheumatol/n4gkgl.
235. Schonenberg-Meinema D, Bergkamp SC, Nassar-Sheikh Rashid A, Gruppen MP, Middelkamp-Hup MA, Armbrust W, et al. Nailfold capillary scleroderma pattern may be associated with disease damage in childhood-onset systemic lupus erythematosus: important lessons from longitudinal follow-up. *Lupus Sci. Med.* **2022**, *9*, e000572. doi:10.1136/lupus-2021-000572.
236. Makarem YS, Selim ZI, Ismail S, Imam Mekki A, Galal H, El Nouby FH. Nailfold capillaroscopy changes in systemic lupus erythematosus patients: Correlation with disease activity and anti-uridin1-ribonucleoprotein antibodies. *Reumatol. Clin.* **2025**, *21*, 501840. doi:10.1016/j.reuma.2025.501840.
237. Gasser P, Meienberg O. Finger microcirculation in classical migraine. A video-microscopic study of nailfold capillaries. *Eur. Neurol.* **1991**, *31*, 168–171. doi:10.1159/000116670.
238. Hegyalijai T, Meienberg O, Dubler B, Gasser P. Cold-induced acral vasospasm in migraine as assessed by nailfold video-microscopy: Prevalence and response to migraine prophylaxis. *Angiology* **1997**, *48*, 345–349. doi:10.1177/000331979704800407.
239. de Villiers S, Bester J, Kell DB, Pretorius E. Erythrocyte health and the possible role of amyloidogenic blood clotting in the evolving haemodynamics of female migraine-with-aura pathophysiology: Results from a pilot study. *Front. Neurol.* **2019**, *10*, 1262. doi:10.3389/fneur.2019.01262.
240. Bourquard A, Pablo-Trinidad A, Butterworth I, Sánchez-Ferro Á, Cerrato C, Humala K, et al. Non-invasive detection of severe neutropenia in chemotherapy patients by optical imaging of nailfold microcirculation. *Sci. Rep.* **2018**, *8*, 5301. doi:10.1038/s41598-018-23591-0.
241. McKay GN, Mohan N, Butterworth I, Bourquard A, Sánchez-Ferro Á, Castro-González C, et al. Visualization of blood cell contrast in nailfold capillaries with high-speed reverse lens mobile phone microscopy. *Biomed. Opt. Express* **2020**, *11*, 2268–2276. doi:10.1364/BOE.382376.
242. Arslan NG, Pancar GS. Nailfold capillaroscopic changes of sleep apnea patients. *Microvasc. Res.* **2021**, *137*, 104177. doi:10.1016/j.mvr.2021.104177.
243. van Vuuren MJ, Nell TA, Carr JA, Kell DB, Pretorius E. Iron dysregulation and inflammagens related to oral and gut health are central to the development of Parkinson's disease. *Biomolecules* **2021**, *11*, 30. doi:10.3390/biom11010030.
244. Ersozlu ED, Bakirci S, Sunu C, Erturk Z, Acikgoz SB, Tamer A. Use of nailfold video capillaroscopy in polycythemia vera. *Arch. Rheumatol.* **2022**, *37*, 404–410. doi:10.46497/ArchRheumatol.2022.9271.
245. Pinal-Fernandez I, Fonollosa-Pla V, Selva-O'Callaghan A. Improvement of the nailfold capillaroscopy after immunosuppressive treatment in polymyositis. *QJM* **2016**, *109*, 205–206. doi:10.1093/qjmed/hcv196.
246. Shenavandeh S, Rashidi F. Nailfold capillaroscopy changes with disease activity in patients with inflammatory myositis including overlap myositis, pure dermatomyositis, and pure polymyositis. *Reumatologia* **2022**, *60*, 42–52. doi:10.5114/reum.2022.114109.
247. Pacini G, Schenone C, Pogna A, Ferraiolo A, Ferrero S, Gustavino C, et al. Full longitudinal nailfold videocapillaroscopy analysis of microvascular changes during normal pregnancy. *Microvasc. Res.* **2022**, *141*, 104343. doi:10.1016/j.mvr.2022.104343.
248. Rusavy Z, Pitrova B, Korecko V, Kalis V. Changes in capillary diameters in pregnancy-induced hypertension. *Hypertens. Pregnancy* **2015**, *34*, 307–313. doi:10.3109/10641955.2015.1033925.
249. Thevissen K, Demir M, Cornette J, Gyselaers W. Nailfold Video Capillaroscopy in Pregnant Women With and Without Cardiovascular Risk Factors. *Front. Med.* **2022**, *9*, 904373. doi:10.3389/fmed.2022.904373.
250. Thevissen K, Gyselaers W. Capillaroscopy in pregnancy. *Expert. Rev. Med. Devices* **2017**, *14*, 961–967. doi:10.1080/17434440.2017.1409113.
251. Graceffa D, Amorosi B, Maiani E, Bonifati C, Chimenti MS, Perricone R, et al. Capillaroscopy in psoriatic and rheumatoid arthritis: a useful tool for differential diagnosis. *Arthritis* **2013**, *2013*, 957480. doi:10.1155/2013/957480.
252. Fink C, Kilian S, Bertlich I, Hoxha E, Bardehle F, Enk A, et al. Evaluation of capillary pathologies by nailfold capillaroscopy in patients with psoriasis vulgaris: study protocol for a prospective, controlled exploratory study. *BMJ Open* **2018**, *8*, e021595. doi:10.1136/bmjopen-2018-021595.
253. Bardehle F, Sies K, Enk A, Rosenberger A, Fink C, Haenssle H. Nailfold videocapillaroscopy identifies microvascular pathologies in psoriasis vulgaris: Results of a prospective controlled study. *J. Dtsch. Dermatol. Ges.* **2021**, *19*, 1736–1744.

- doi:10.1111/ddg.14606.
254. Lazar LT, Guldberg-Moller J, Lazar BT, Mogensen M. Nailfold capillaroscopy as diagnostic test in patients with psoriasis and psoriatic arthritis: A systematic review. *Microvasc. Res.* **2023**, *147*, 104476. doi:10.1016/j.mvr.2023.104476.
 255. Cafaro G, Bursi R, Valentini V, Hansel K, Perricone C, Venerito V, et al. Combined semiquantitative nail-entheses complex ultrasonography and capillaroscopy in psoriasis and psoriatic arthritis. *Front. Immunol.* **2024**, *15*, 1505322. doi:10.3389/fimmu.2024.1505322.
 256. Santhosh P, Riyaz N, Bagde P, Binitha MP, Sasidharanpillai S. A Cross-Sectional Study of Nailfold Capillary Changes in Psoriasis. *Indian Dermatol. Online J.* **2021**, *12*, 873–878. doi:10.4103/idoj.IDOJ_793_20.
 257. Sivasankari M, Arora S, Vasdev V, Mary EM. Nailfold capillaroscopy in psoriasis. *Med. J. Armed Forces India* **2021**, *77*, 75–81. doi:10.1016/j.mjafi.2020.01.013.
 258. Smits AJ, Isebia K, Combee-Duffy C, van der Wal S, Nossent EJ, Boonstra A, et al. Low nailfold capillary density in patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: biomarker of clinical outcome? *Sci. Rep.* **2024**, *14*, 19467. doi:10.1038/s41598-024-69017-y.
 259. Sugimoto T, Dohi Y, Yoshida Y, Mokuda S, Hirata S. Ameliorated nailfold capillary morphology of patients with pulmonary arterial hypertension in systemic sclerosis, treated with riociguat. *Rheumatol. Adv. Pract.* **2023**, *7*, rkad011. doi:10.1093/rap/rkad011.
 260. Brunner-Ziegler S, Dassler E, Muller M, Pratscher M, Forstner NFM, Koppensteiner R, et al. Capillaroscopic differences between primary Raynaud phenomenon and healthy controls indicate potential microangiopathic involvement in benign vasospasms. *Vasc. Med.* **2024**, *29*, 200–207. doi:10.1177/1358863X231223523.
 261. Kapten K, Orczyk K, Smolewska E. The effect of vitamin D3 and thyroid hormones on the capillaroscopy-confirmed microangiopathy in pediatric patients with a suspicion of systemic connective tissue disease—a single-center experience with Raynaud phenomenon. *Rheumatol. Int.* **2021**, *41*, 1485–1493. doi:10.1007/s00296-021-04919-y.
 262. Koenig M, Joyal F, Fritzler MJ, Roussin A, Abrahamowicz M, Boire G, et al. Autoantibodies and microvascular damage are independent predictive factors for the progression of Raynaud's phenomenon to systemic sclerosis: A twenty-year prospective study of 586 patients, with validation of proposed criteria for early systemic sclerosis. *Arthritis Rheum.* **2008**, *58*, 3902–3912. doi:10.1002/art.24038.
 263. Smith V, Vanhaecke A, Herrick AL, Distler O, Guerra MG, Denton CP, et al. Fast track algorithm: How to differentiate a “scleroderma pattern” from a “non-scleroderma pattern”. *Autoimmun. Rev.* **2019**, *18*, 102394. doi:10.1016/j.autrev.2019.102394.
 264. Nawaz I, Nawaz Y, Nawaz E, Manan MR, Mahmood A. Raynaud's Phenomenon: Reviewing the Pathophysiology and Management Strategies. *Cureus* **2022**, *14*, e21681. doi:10.7759/cureus.21681.
 265. Roberts-Thomson PJ, Patterson KA, Walker JG. Clinical utility of nailfold capillaroscopy. *Intern. Med. J.* **2023**, *53*, 671–679. doi:10.1111/imj.15966.
 266. Amaral MC, Paula FS, Caetano J, Ames PR, Alves JD. Re-evaluation of nailfold capillaroscopy in discriminating primary from secondary Raynaud's phenomenon and in predicting systemic sclerosis: A randomised observational prospective cohort study. *Expert. Rev. Clin. Immunol.* **2024**, *20*, 665–672. doi:10.1080/1744666X.2024.2313642.
 267. Wu PC, Huang MN, Kuo YM, Hsieh SC, Yu CL. Clinical applicability of quantitative nailfold capillaroscopy in differential diagnosis of connective tissue diseases with Raynaud's phenomenon. *J. Formos. Med. Assoc.* **2013**, *112*, 482–488. doi:10.1016/j.jfma.2012.02.029.
 268. Herrick AL, Wigley FM. Raynaud's phenomenon. *Best. Pract. Res. Clin. Rheumatol.* **2020**, *34*, 101474. doi:10.1016/j.berh.2019.101474.
 269. Herrick AL, Dinsdale G, Murray A. New perspectives in the imaging of Raynaud's phenomenon. *Eur. J. Rheumatol.* **2020**, *7*, S212–S221. doi:10.5152/eurjrheum.2020.19124.
 270. van Roon AM, Smit AJ, van Roon AM, Bootsma H, Mulder DJ. Digital ischaemia during cooling is independently related to nailfold capillaroscopic pattern in patients with Raynaud's phenomenon. *Rheumatology* **2016**, *55*, 1083–1090. doi:10.1093/rheumatology/kew028.
 271. Screm G, Mondini L, Salton F, Confalonieri P, Bozzi C, Torregiani C, et al. Assessment of Treatment Effects of Aminaphtone by Capillaroscopy in a Patient with Raynaud's Phenomenon. *Pharmaceuticals* **2025**, *18*, 203. doi:10.3390/ph18020203.
 272. do Rosário e Souza EJ, Kayser C. Nailfold capillaroscopy: relevance to the practice of rheumatology. *Rev. Bras. Reumatol.* **2015**, *55*, 264–271. doi:10.1016/j.rbr.2014.09.003.
 273. Chojnowski MM, Felis-Giemza A, Olesińska M. Capillaroscopy—a role in modern rheumatology. *Reumatologia* **2016**, *54*, 67–72. doi:10.5114/reum.2016.60215.
 274. Anyfanti P, Angeloudi E, Dara A, Arvanitaki A, Bekiari E, Kitas GD, et al. Nailfold Videocapillaroscopy for the Evaluation of Peripheral Microangiopathy in Rheumatoid Arthritis. *Life* **2022**, *12*, 1167. doi:10.3390/life12081167.
 275. Eden M, Wilkinson S, Murray A, Bharathi PG, Vail A, Taylor CJ, et al. Nailfold capillaroscopy: A survey of current UK practice and 'next steps' to increase uptake among rheumatologists. *Rheumatology* **2022**, *62*, 335–340. doi:10.1093/rheumatology/keac320.

276. Ingegnoli F, Cornalba M, De Angelis R, Guiducci S, Giuggioli D, Pizzorni C, et al. Nailfold capillaroscopy in the rheumatological current clinical practice in Italy: results of a national survey. *Reumatismo* **2022**, *74*, 97–102. doi:10.4081/reumatismo.2022.1508.
277. Angeloudi E, Anyfanti P, Dara A, Pagkopoulou E, Bekiari E, Sgouropoulou V, et al. Peripheral nailfold capillary microscopic abnormalities in rheumatoid arthritis are associated with arterial stiffness: Results from a cross-sectional study. *Microvasc. Res.* **2023**, *150*, 104576. doi:10.1016/j.mvr.2023.104576.
278. Anghel D, Sirbu CA, Petrache OG, Opris-Belinski D, Negru MM, Bojinca VC, et al. Nailfold Videocapillaroscopy in Patients with Rheumatoid Arthritis and Psoriatic Arthropathy on ANTI-TNF-ALPHA Therapy. *Diagnostics* **2023**, *13*, 2079. doi:10.3390/diagnostics13122079.
279. Schonenberg-Meinema D, Cutolo M, Smith V. Capillaroscopy in the daily clinic of the pediatric rheumatologist. *Best. Pract. Res. Clin. Rheumatol.* **2024**, *38*, 101978. doi:10.1016/j.berh.2024.101978.
280. Anghel D, Prioteasă OG, Nicolau IN, Bucurică S, Belinski DO, Popescu GG, et al. The Role of Nailfold Videocapillaroscopy in the Diagnosis and Monitoring of Interstitial Lung Disease Associated with Rheumatic Autoimmune Diseases. *Diagnostics* **2025**, *15*, 362. doi:10.3390/diagnostics15030362.
281. Bezuidenhout J, Venter C, Roberts T, Tarr G, Kell D, Pretorius E. The Atypical Fibrin Fibre Network in Rheumatoid Arthritis and its Relation to Autoimmunity, Inflammation and Thrombosis. *bioRxiv* **2020**, 2020-05. doi:10.1101/2020.05.28.121301.
282. Pretorius E, Oberholzer HM, van der Spuy WJ, Swanepoel AC, Soma P. Scanning electron microscopy of fibrin networks in rheumatoid arthritis: A qualitative analysis. *Rheumatol. Int.* **2012**, *32*, 1611–1615. doi:10.1007/s00296-011-1805-2.
283. Acemoğlu ŞŞZ, Türk I, Aşık MA, Bircan AÖ, Deniz PP, Arslan D, et al. Microvascular damage evaluation based on nailfold videocapillaroscopy in sarcoidosis. *Clin. Rheumatol.* **2023**, *42*, 1951–1957. doi:10.1007/s10067-023-06582-z.
284. Cattelan F, Hysa E, Gotelli E, Pizzorni C, Bica PF, Grosso M, et al. Microvascular capillaroscopic abnormalities and occurrence of antinuclear autoantibodies in patients with sarcoidosis. *Rheumatol. Int.* **2022**, *42*, 2199–2210. doi:10.1007/s00296-022-05190-5.
285. Chianese M, Screm G, Confalonieri P, Salton F, Trotta L, Da Re B, et al. Nailfold Video-Capillaroscopy in Sarcoidosis: New Perspectives and Challenges. *Tomography* **2024**, *10*, 1547–1563. doi:10.3390/tomography10100114.
286. Paolino S, Goegan F, Cimmino MA, Casabella A, Pizzorni C, Patane M, et al. Advanced microvascular damage associated with occurrence of sarcopenia in systemic sclerosis patients: results from a retrospective cohort study. *Clin. Exp. Rheumatol.* **2020**, *38* (Suppl 125), 65–72.
287. Zhang L, Mao D, Zhang Q. Correlation between sarcopenia and nailfold microcirculation, serum 25-hydroxycholecalciferol (vitamin D3) and IL-17 levels in female patients with rheumatoid arthritis. *Biomed. Pap. Med. Fac. Univ. Palacky. Olomouc. Czech Repub.* **2021**, *165*, 264–269. doi:10.5507/bp.2020.036.
288. Miranda M, Balarini M, Caixeta D, Bouskela E. Microcirculatory dysfunction in sepsis: Pathophysiology, clinical monitoring, and potential therapies. *Am. J. Physiol. Heart Circ. Physiol.* **2016**, *311*, H24–H35. doi:10.1152/ajpheart.00034.2016.
289. Kell DB, Pretorius E. To what extent are the terminal stages of sepsis, septic shock, SIRS, and multiple organ dysfunction syndrome actually driven by a toxic prion/amyloid form of fibrin? *Semin. Thromb. Hemost.* **2018**, *44*, 224–238. doi:10.1055/s-0037-1604108.
290. De Backer D, Creteur J, Preiser JC, Dubois MJ, Vincent JL. Microvascular blood flow is altered in patients with sepsis. *Am. J. Respir. Crit. Care Med.* **2002**, *166*, 98–104. doi:10.1164/rccm.200109-016oc.
291. Sapozhnikov M, Rehman M, Johnson C, Daich J, Saliccioli L, Gillette P, et al. Characterization of microvascular disease in patients with sickle cell disease using nailfold capillaroscopy. *Microvasc. Res.* **2019**, *125*, 103877. doi:10.1016/j.mvr.2019.04.007.
292. Melsens K, Leone MC, Paolino S, Elewaut D, Gerli R, Vanhaecke A, et al. Nailfold capillaroscopy in Sjögren's syndrome: a systematic literature review and standardised interpretation. *Clin. Exp. Rheumatol.* **2020**, *38* (Suppl 126), 150–157.
293. Lercara A, Malattia C, Hysa E, Gattorno M, Cere A, Lavarello C, et al. Microvascular status in juvenile Sjögren's disease: the first nailfold videocapillaroscopy investigation. *Clin. Rheumatol.* **2024**, *43*, 733–741. doi:10.1007/s10067-023-06857-5.
294. Soulaïdopoulos S, Triantafyllidou E, Garyfallos A, Kitas GD, Dimitroulas T. The role of nailfold capillaroscopy in the assessment of internal organ involvement in systemic sclerosis: A critical review. *Autoimmun. Rev.* **2017**, *16*, 787–795. doi:10.1016/j.autrev.2017.05.019.
295. Paxton D, Pauling JD. Does nailfold capillaroscopy help predict future outcomes in systemic sclerosis? A systematic literature review. *Semin. Arthritis Rheum.* **2018**, *48*, 482–494. doi:10.1016/j.semarthrit.2018.02.005.
296. Nikolova Lambova S, Müller-Ladner U. Nailfold capillaroscopy in systemic sclerosis—State of the art: The evolving knowledge about capillaroscopic abnormalities in systemic sclerosis. *J. Scleroderma Relat. Disord.* **2019**, *4*, 200–211. doi:10.1177/2397198319833486.
297. Smith V, Vanhaecke A, Vandecasteele E, Guerra M, Paolino S, Melsens K, et al. Nailfold Videocapillaroscopy in Systemic Sclerosis-related Pulmonary Arterial Hypertension: A Systematic Literature Review. *J. Rheumatol.* **2020**, *47*, 888–895. doi:10.3899/jrheum.190296.
298. Paolino S, Gotelli E, Goegan F, Casabella A, Ferrari G, Patane M, et al. Body composition and bone status in relation to

- microvascular damage in systemic sclerosis patients. *J. Endocrinol. Investig.* **2021**, *44*, 255–264. doi:10.1007/s40618-020-01234-4.
299. van Leeuwen NM, Ciaffi J, Schoones JW, Huizinga TWJ, de Vries-Bouwstra JK. Contribution of Sex and Autoantibodies to Microangiopathy Assessed by Nailfold Videocapillaroscopy in Systemic Sclerosis: A Systematic Review of the Literature. *Arthritis Care Res.* **2021**, *73*, 722–731. doi:10.1002/acr.24149.
 300. Minopoulou I, Theodorakopoulou M, Boutou A, Arvanitaki A, Pitsiou G, Doumas M, et al. Nailfold Capillaroscopy in Systemic Sclerosis Patients with and without Pulmonary Arterial Hypertension: A Systematic Review and Meta-Analysis. *J. Clin. Med.* **2021**, *10*, 1528. doi:10.3390/jcm10071528.
 301. Mandujano A, Golubov M. Animal Models of Systemic Sclerosis: Using Nailfold Capillaroscopy as a Potential Tool to Evaluate Microcirculation and Microangiopathy: A Narrative Review. *Life* **2022**, *12*, 703. doi:10.3390/life12050703.
 302. Hysa E, Campitiello R, Sammori S, Gotelli E, Cere A, Pesce G, et al. Specific Autoantibodies and Microvascular Damage Progression Assessed by Nailfold Videocapillaroscopy in Systemic Sclerosis: Are There Peculiar Associations? An Update. *Antibodies* **2023**, *12*, 3. doi:10.3390/antib12010003.
 303. Ma Z, Mulder DJ, Gniadecki R, Cohen Tervaert JW, Osman M. Methods of Assessing Nailfold Capillaroscopy Compared to Video Capillaroscopy in Patients with Systemic Sclerosis-A Critical Review of the Literature. *Diagnostics* **2023**, *13*, 2204. doi:10.3390/diagnostics13132204.
 304. De Angelis R, Ricciari V, Cipolletta E, Del Papa N, Ingegnoli F, Bosello S, et al. Significant nailfold capillary loss and late capillaroscopic pattern are associated with pulmonary arterial hypertension in systemic sclerosis. *Rheumatology* **2024**, *63*, 1616–1623. doi:10.1093/rheumatology/kead445.
 305. Zanatta E, Famoso G, Boscain F, Montisci R, Pigatto E, Polito P, et al. Nailfold avascular score and coronary microvascular dysfunction in systemic sclerosis: A newsworthy association. *Autoimmun. Rev.* **2019**, *18*, 177–183. doi:10.1016/j.autrev.2018.09.002.
 306. Elsayed SA, Mounir A, Mostafa EM, Saif DS, Mounir O. The correlation between retinal microvascular changes by optical coherence tomography angiography and nailfold capillaroscopic findings in patients with systemic sclerosis. *J Rheum Dis.* **2025**, *32*, 198–210. doi.org/10.4078/jrd.2024.0124.
 307. Hammada RM, El-Gharbawy NH, Khalifa AA, Moharram AA, Elziaty RA. Neutrophil-to-lymphocyte ratio: association with microcirculatory changes detected by nailfold capillaroscopy in scleroderma patients and its relation to disease severity. *Egyptian Rheumatol. Rehab.* **2024**, *52*, 4. doi:10.1186/s43166-024-00299-w.
 308. Vanhaecke A, Cutolo M, Distler O, Ricciari V, Allanore Y, Denton CP, et al. Nailfold capillaroscopy in SSc: innocent bystander or promising biomarker for novel severe organ involvement/progression? *Rheumatology* **2022**, *61*, 4384–4396. doi:10.1093/rheumatology/keac079.
 309. Smith V, Vanhaecke A, Guerra MG, Melsens K, Vandecasteele E, Paolino S, et al. May capillaroscopy be a candidate tool in future algorithms for SSC-ILD: Are we looking for the holy grail? A systematic review. *Autoimmun. Rev.* **2020**, *19*, 102619. doi:10.1016/j.autrev.2020.102619.
 310. Andracco R, Irace R, Zaccara E, Vettori S, Maglione W, Riccardi A, et al. The cumulative number of micro-haemorrhages and micro-thromboses in nailfold videocapillaroscopy is a good indicator of disease activity in systemic sclerosis: A validation study of the NEMO score. *Arthritis Res. Ther.* **2017**, *19*, 133. doi:10.1186/s13075-017-1354-5.
 311. Pignataro F, Maglione W, Minniti A, Sambataro D, Sambataro G, Campanaro F, et al. NEMO score in nailfold videocapillaroscopy is a good tool to assess both steady state levels and overtime changes of disease activity in patients with systemic sclerosis: A comparison with the proposed composite indices for this disease status entity. *Arthritis Res. Ther.* **2019**, *21*, 258. doi:10.1186/s13075-019-2032-6.
 312. Del Papa N, Pignataro F, Maglione W, Minniti A, Sambataro D, Sambataro G, et al. High NEMO score values in nailfold videocapillaroscopy are associated with the subsequent development of ischaemic digital ulcers in patients with systemic sclerosis. *Arthritis Res. Ther.* **2020**, *22*, 237. doi:10.1186/s13075-020-02342-5.
 313. Crescenzi D, Balducci D, Mazzetti M, Menghini D, Gelardi C, Pedini V, et al. Use of nailfold capillaroscopy for the early diagnosis of systemic sclerosis in patients with primary biliary cholangitis. *Ann. Gastroenterol.* **2025**, *38*, 187–194. doi:10.20524/aog.2025.0949.
 314. Ricciari V, Vasile M, Iannace N, Stefanantoni K, Sciarra I, Vizza CD, et al. Systemic sclerosis patients with and without pulmonary arterial hypertension: a nailfold capillaroscopy study. *Rheumatology* **2013**, *52*, 1525–1528. doi:10.1093/rheumatology/ket168.
 315. Lim MWS, Setjiadi D, Dobbin SJH, Lang NN, Delles C, Connelly PJ. Nailfold video-capillaroscopy in the study of cardiovascular disease: a systematic review. *Blood Press. Monit.* **2023**, *28*, 24–32. doi:10.1097/MBP.0000000000000624.
 316. Cutolo M, Sulli A, Secchi ME, Paolino S, Pizzorni C. Nailfold capillaroscopy is useful for the diagnosis and follow-up of autoimmune rheumatic diseases. A future tool for the analysis of microvascular heart involvement? *Rheumatology* **2006**, *45*, iv43–iv46. doi:10.1093/rheumatology/ke1310.
 317. Chang CH, Tsai RK, Wu WC, Kuo SL, Yu HS. Use of dynamic capillaroscopy for studying cutaneous microcirculation in patients with diabetes mellitus. *Microvasc. Res.* **1997**, *53*, 121–127. doi:10.1006/mvre.1996.2003.

318. Hahn M, Heubach T, Steins A, Jünger M. Hemodynamics in nailfold capillaries of patients with systemic scleroderma: Synchronous measurements of capillary blood pressure and red blood cell velocity. *J. Invest. Dermatol.* **1998**, *110*, 982–985. doi:10.1046/j.1523-1747.1998.00190.x.
319. Mugii N, Hasegawa M, Hamaguchi Y, Tanaka C, Kaji K, Komura K, et al. Reduced red blood cell velocity in nail-fold capillaries as a sensitive and specific indicator of microcirculation injury in systemic sclerosis. *Rheumatology* **2009**, *48*, 696–703. doi:10.1093/rheumatology/kep066.
320. Wu CC, Zhang G, Huang TC, Lin KP. Red blood cell velocity measurements of complete capillary in finger nail-fold using optical flow estimation. *Microvasc. Res.* **2009**, *78*, 319–324. doi:10.1016/j.mvr.2009.07.002.
321. Wu CC, Lin WC, Zhang G, Chang CW, Liu RS, Lin KP, et al. Accuracy evaluation of RBC velocity measurement in nail-fold capillaries. *Microvasc. Res.* **2011**, *81*, 252–260. doi:10.1016/j.mvr.2011.01.003.
322. Maranhão PA, Coelho de Souza MdG, Kraemer-Aguiar LG, Bouskela E. Dynamic nailfold videocapillaroscopy may be used for early detection of microvascular dysfunction in obesity. *Microvasc. Res.* **2016**, *106*, 31–35. doi:10.1016/j.mvr.2016.03.004.
323. Niizawa T, Yokemura K, Kusaka T, Sugashi T, Miura I, Kawagoe K, et al. Automated capillary flow segmentation and mapping for nailfold video capillaroscopy. *Microcirculation* **2022**, *29*, e12753. doi:10.1111/micc.12753.
324. Chen S, Wei D, Gu S, Yang Z. Blood flow characterization in nailfold capillary using optical flow-assisted two-stream network and spatial-temporal image. *Biomed. Phys. Eng. Express* **2023**, *9*, 045023. doi:10.1088/2057-1976/acdb7c.
325. Pakbin M, Hejazi SM, Najafizadeh SR. Quantitative nail fold capillary blood flow using capillaroscopy system and ImageJ software in healthy individuals. *Front. Biomed. Technol.* **2023**, *10*, 38–46. doi:10.18502/ftb.v10i1.11511.
326. Dremine V, Volkov M, Margaryants N, Myalitsin D, Rafailov E, Dunaev A. Blood flow dynamics in the arterial and venous parts of the capillary. *J. Biomech.* **2025**, *179*, 112482. doi:10.1016/j.jbiomech.2024.112482.
327. Callard F, Perego E. How and why patients made Long Covid. *Soc. Sci. Med.* **2021**, *268*, 113426. doi:10.1016/j.socscimed.2020.113426.
328. Al-Aly Z, Topol E. Solving the puzzle of Long Covid. *Science* **2024**, *383*, 830–832. doi:10.1126/science.adl0867.
329. Al-Aly Z, Davis H, McCorkell L, Soares L, Wulf-Hanson S, Iwasaki A, Topol EJ. Long COVID science, research and policy. *Nat. Med.* **2024**, *30*, 2148–2164. doi:10.1038/s41591-024-03173-6.
330. Aiyegbusi OL, Hughes SE, Turner G, Rivera SC, McMullan C, Chandan JS, et al. Symptoms, complications and management of long COVID: a review. *J. R. Soc. Med.* **2021**, *114*, 428–442. doi:10.1177/01410768211032850.
331. Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequelae of COVID-19. *Nature* **2021**, *594*, 259–264. doi:10.1038/s41586-021-03553-9.
332. Hayes LD, Ingram J, Sculthorpe NF. More Than 100 Persistent Symptoms of SARS-CoV-2 (Long COVID): A Scoping Review. *Front. Med.* **2021**, *8*, 750378. doi:10.3389/fmed.2021.750378.
333. Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: Major findings, mechanisms and recommendations. *Nat. Rev. Microbiol.* **2023**, *21*, 133–146. doi:10.1038/s41579-022-00846-2.
334. Nalbandian A, Desai AD, Wan EY. Post-COVID-19 Condition. *Annu. Rev. Med.* **2023**, *74*, 55–64. doi:10.1146/annurev-med-043021-030635.
335. Greenhalgh T, Sivan M, Perlowski A, Nikolich JŽ. Long COVID: A clinical update. *Lancet* **2024**, *404*, 707–724. doi:10.1016/S0140-6736(24)01136-X.
336. Komaroff AL, Lipkin WI. ME/CFS and Long COVID share similar symptoms and biological abnormalities: Road map to the literature. *Front. Med.* **2023**, *10*, 1187163. doi:10.3389/fmed.2023.1187163.
337. Poole-Wright K, Guennouni I, Sterry O, Evans RA, Gaughran F, Chalder T. Fatigue outcomes following COVID-19: a systematic review and meta-analysis. *BMJ Open* **2023**, *13*, e063969. doi:10.1136/bmjopen-2022-063969.
338. Chang JC. Sepsis and septic shock: endothelial molecular pathogenesis associated with vascular microthrombotic disease. *Thromb. J.* **2019**, *17*, 10. doi:10.1186/s12959-019-0198-4.
339. Guven G, Hilty MP, Ince C. Microcirculation: Physiology, Pathophysiology, and Clinical Application. *Blood Purif.* **2020**, *49*, 143–150. doi:10.1159/000503775.
340. Wei JX, Jiang HL, Chen XH. Endothelial cell metabolism in sepsis. *World J. Emerg. Med.* **2023**, *14*, 10–16. doi:10.5847/wjem.j.1920-8642.2023.019.
341. Cusack R, O'Neill S, Martin-Loeches I. Effects of Fluids on the Sublingual Microcirculation in Sepsis. *J. Clin. Med.* **2022**, *11*, 7277. doi:10.3390/jcm11247277.
342. Ince C. The microcirculation is the motor of sepsis. *Crit. Care* **2005**, *9* (Suppl 4), S13–S19. doi:10.1186/cc3753.
343. Lipińska-Gediga M. Sepsis and septic shock-is a microcirculation a main player? *Anaesthesiol. Intensive Ther.* **2016**, *48*, 261–265. doi:10.5603/AIT.a2016.0037.
344. De Backer D, Ricottilli F, Ospina-Tascón GA. Septic shock: A microcirculation disease. *Curr. Opin. Anaesthesiol.* **2021**, *34*, 85–91. doi:10.1097/ACO.0000000000000957.
345. De Backer D. Novelty in the evaluation of microcirculation in septic shock. *J. Intensive Med.* **2023**, *3*, 124–130. doi:10.1016/j.jointm.2022.09.002.
346. Guo Q, Liu D, Wang X, Chinese Critical Ultrasound Study Group. Early peripheral perfusion monitoring in septic shock. *Eur.*

- J. Med. Res.* **2024**, *29*, 477. doi:10.1186/s40001-024-02074-1.
347. Wang H, Ding H, Wang ZY, Zhang K. Research progress on microcirculatory disorders in septic shock: A narrative review. *Medicine* **2024**, *103*, e37273. doi:10.1097/MD.00000000000037273.
 348. Chua MT, Kuan WS. Venous-to-arterial carbon dioxide differences and the microcirculation in sepsis. *Ann. Transl. Med.* **2016**, *4*, 62. doi:10.3978/j.issn.2305-5839.2015.12.55.
 349. Colbert JF, Schmidt EP. Endothelial and Microcirculatory Function and Dysfunction in Sepsis. *Clin. Chest Med.* **2016**, *37*, 263–275. doi:10.1016/j.ccm.2016.01.009.
 350. Charlton M, Sims M, Coats T, Thompson JP. The microcirculation and its measurement in sepsis. *J. Intensive Care Soc.* **2017**, *18*, 221–227. doi:10.1177/1751143716678638.
 351. Duranteau J, De Backer D, Donadello K, Shapiro NI, Hutchings SD, Rovas A, et al. The future of intensive care: the study of the microcirculation will help to guide our therapies. *Crit. Care* **2023**, *27*, 190. doi:10.1186/s13054-023-04474-x.
 352. Hawiger J, Veach RA, Zienkiewicz J. New paradigms in sepsis: from prevention to protection of failing microcirculation. *J. Thromb. Haemost.* **2015**, *13*, 1743–1756. doi:10.1111/jth.13061.
 353. Opal SM, van der Poll T. Endothelial barrier dysfunction in septic shock. *J. Intern. Med.* **2015**, *277*, 277–293. doi:10.1111/joim.12331.
 354. Potter EK, Hodgson L, Creagh-Brown B, Forni LG. Manipulating the Microcirculation in Sepsis—the Impact of Vasoactive Medications on Microcirculatory Blood Flow: A Systematic Review. *Shock* **2019**, *52*, 5–12. doi:10.1097/SHK.0000000000001239.
 355. Colantuoni A, Martini R, Caprari P, Ballestri M, Capecchi PL, Gnasso A, et al. COVID-19 Sepsis and Microcirculation Dysfunction. *Front. Physiol.* **2020**, *11*, 747. doi:10.3389/fphys.2020.00747.
 356. Tang AL, Shen MJ, Zhang GQ. Intestinal microcirculation dysfunction in sepsis: pathophysiology, clinical monitoring, and therapeutic interventions. *World J. Emerg. Med.* **2022**, *13*, 343–348. doi:10.5847/wjem.j.1920-8642.2022.031.
 357. Yajnik V, Maarouf R. Sepsis and the microcirculation: the impact on outcomes. *Curr. Opin. Anaesthesiol.* **2022**, *35*, 230–235. doi:10.1097/ACO.0000000000001098.
 358. Vallet B. Bench-to-bedside review: endothelial cell dysfunction in severe sepsis: A role in organ dysfunction? *Crit. Care* **2003**, *7*, 130–138. doi:10.1186/cc1864.
 359. Xing K, Murthy S, Liles WC, Singh JM. Clinical utility of biomarkers of endothelial activation in sepsis—a systematic review. *Crit. Care* **2012**, *16*, R7. doi:10.1186/cc11145.
 360. Spronk PE, Zandstra DF, Ince C. Bench-to-bedside review: sepsis is a disease of the microcirculation. *Crit. Care* **2004**, *8*, 462–468. doi:10.1186/cc2894.
 361. Joffe J, Hellman J. Oxidative Stress and Endothelial Dysfunction in Sepsis and Acute Inflammation. *Antioxid. Redox Signal* **2021**, *35*, 1291–1307. doi:10.1089/ars.2021.0027.
 362. Joffe J, Hellman J, Ince C, Ait-Oufella H. Endothelial Responses in Sepsis. *Am. J. Respir. Crit. Care Med.* **2020**, *202*, 361–370. doi:10.1164/rccm.201910-1911TR.
 363. Dolmatova EV, Wang K, Mandavilli R, Griendling KK. The effects of sepsis on endothelium and clinical implications. *Cardiovasc. Res.* **2021**, *117*, 60–73. doi:10.1093/cvr/cvaa070.
 364. Damiani E, Carsetti A, Casarotta E, Domizi R, Scorcella C, Donati A, et al. Microcirculation-guided resuscitation in sepsis: the next frontier? *Front. Med.* **2023**, *10*, 1212321. doi:10.3389/fmed.2023.1212321.
 365. Dilken O, Ergin B, Ince C. Assessment of sublingual microcirculation in critically ill patients: Consensus and debate. *Ann. Transl. Med.* **2020**, *8*, 793. doi:10.21037/atm.2020.03.222.
 366. Tang A, Shi Y, Dong Q, Wang S, Ge Y, Wang C, et al. Prognostic Value of Sublingual Microcirculation in Sepsis: A Systematic Review and Meta-analysis. *J. Intensive Care Med.* **2024**, *39*, 1221–1230. doi:10.1177/08850666241253800.
 367. Ahmed S, Zimba O, Gasparyan AY. Thrombosis in Coronavirus disease 2019 (COVID-19) through the prism of Virchow's triad. *Clin. Rheumatol.* **2020**, *39*, 2529–2543. doi:10.1007/s10067-020-05275-1.
 368. Wolberg AS, Aleman MM, Leiderman K, Machlus KR. Procoagulant activity in hemostasis and thrombosis: Virchow's triad revisited. *Anesth. Analg.* **2012**, *114*, 275–285. doi:10.1213/ANE.0b013e31823a088c.
 369. Luo X, Xie J, Huang L, Gan W, Chen M. Efficacy and safety of activating blood circulation and removing blood stasis of Traditional Chinese Medicine for managing renal fibrosis in patients with chronic kidney disease: A systematic review and Meta-analysis. *J. Tradit. Chin. Med.* **2023**, *43*, 429–440. doi:10.19852/j.cnki.jtcm.20230308.003.
 370. Chen KJ. Blood stasis syndrome and its treatment with activating blood circulation to remove blood stasis therapy. *Chin. J. Integr. Med.* **2012**, *18*, 891–896. doi:10.1007/s11655-012-1291-5.
 371. Liao J, Wang J, Liu Y, Li J, Duan L, Chen G, et al. Modern researches on Blood Stasis syndrome 1989–2015: A bibliometric analysis. *Medicine* **2016**, *95*, e5533. doi:10.1097/MD.0000000000005533.
 372. Yan J, Dong Y, Niu L, Cai J, Jiang L, Wang C, et al. Clinical effect of Chinese herbal medicine for removing blood stasis combined with acupuncture on sequelae of cerebral infarction. *Am. J. Transl. Res.* **2021**, *13*, 10843–10849.
 373. Rosenthal L, Hernandez P, Vaamonde D. Traditional Chinese medicine, Ayurveda, and fertility. *Fertil. Pregnancy Wellness* **2022**, 209–247. doi:10.1016/B978-0-12-818309-0.00014-9.

374. Birch S, Alraek T, Lee MS, Lee JA, Kim T-H. Understanding blood stasis in traditional East Asian medicine: a comparison of Asian and Western sources. *Eur. J. Integr. Med.* **2021**, *44*, 101341. doi:10.1016/j.eujim.2021.101341.
375. Zhai X, Wang X, Wang L, Xiu L, Wang W, Pang X. Treating Different Diseases with the Same Method-A Traditional Chinese Medicine Concept Analyzed for Its Biological Basis. *Front. Pharmacol.* **2020**, *11*, 946. doi:10.3389/fphar.2020.00946.
376. Yan D-X. *Aging and Blood Stasis: A New TCM Approach to Geriatrics*; Blue Poppy Press: Boulder, CO, USA, 2015.
377. Ishida H, Takamatsu M, Tsuji K, Kosuge T. Studies on active substances in herbs used for oketsu (“stagnant blood”) in Chinese medicine. V. On the anticoagulative principle in moutan cortex. *Chem. Pharm. Bull.* **1987**, *35*, 846–848. doi:10.1248/cpb.35.846.
378. Matsumoto C, Kojima T, Ogawa K, Kamegai S, Oyama T, Shibagaki Y, et al. A proteomic approach for the diagnosis of ‘Oketsu’ (blood stasis), a pathophysiologic concept of Japanese traditional (Kampo) medicine. *Evid. Based Complement. Altern. Med.* **2008**, *5*, 463–474. doi:10.1093/ecam/nem049.
379. Morita A, Murakami A, Watanabe Y, Tamura Y, Suganami A, Shiko Y, et al. The association in Kampo medicine between Oketsu (blood stasis) and sublingual vein width of the tongue on a tongue image analyzing system. *Tradit. Kampo Med.* **2020**, *7*, 108–112. doi:10.1002/tkm2.1243.
380. Morita A, Murakami A, Noguchi K, Watanabe Y, Nakaguchi T, Ochi S, et al. Combination image analysis of tongue color and sublingual vein improves the diagnostic accuracy of Oketsu (blood stasis) in Kampo medicine. *Front. Med.* **2021**, *8*, 790542. doi:10.3389/fmed.2021.790542.
381. Park B, You S, Jung J, Lee JA, Yun KJ, Lee MS. Korean studies on blood stasis: an overview. *Evid. Based Complement. Altern. Med.* **2015**, *2015*, 316872. doi:10.1155/2015/316872.
382. Yi M, Li Q, Zhao Y, Nie S, Wu N, Wang D. Metabolomics study on the therapeutic effect of traditional Chinese medicine Xue-Fu-Zhu-Yu decoction in coronary heart disease based on LC-Q-TOF/MS and GC-MS analysis. *Drug Metab. Pharmacokinet.* **2019**, *34*, 340–349. doi:10.1016/j.dmpk.2019.07.004.
383. Zhao Y, Nie S, Yi M, Wu N, Wang W, Zhang Z, et al. UPLC-QTOF/MS-based metabolomics analysis of plasma reveals an effect of Xue-Fu-Zhu-Yu capsules on blood-stasis syndrome in CHD rats. *J. Ethnopharmacol.* **2019**, *241*, 111908. doi:10.1016/j.jep.2019.111908.
384. He H, Chen G, Gao J, Liu Y, Zhang C, Liu C, et al. Xue-Fu-Zhu-Yu capsule in the treatment of qi stagnation and blood stasis syndrome: a study protocol for a randomised controlled pilot and feasibility trial. *Trials* **2018**, *19*, 515. doi:10.1186/s13063-018-2908-9.
385. Chen S, Wu X, Li T, Cheng W, Han X, Li Y, et al. The Improvement of Cardiac and Endothelial Functions of Xue-Fu-Zhu-Yu Decoction for Patients with Acute Coronary Syndrome: A Meta-Analysis of Randomized Controlled Trials. *Evid. Based Complement. Altern. Med.* **2022**, *2022*, 2671343. doi:10.1155/2022/2671343.
386. Xue DJ, Zhen Z, Wang KX, Zhao JL, Gao Y, Chen YP, et al. Uncovering the potential mechanism of Xue Fu Zhu Yu Decoction in the treatment of intracerebral hemorrhage. *BMC Complement. Med. Ther.* **2022**, *22*, 103. doi:10.1186/s12906-022-03577-2.
387. Kuo CE, Hsu SF, Chen CC, Wu SY, Hung YC, Hsu CY, et al. Prescription characteristics of Xue-Fu-Zhu-Yu-Tang in pain management: a population-based study using the National Health Insurance Research Database in Taiwan. *Front. Pharmacol.* **2023**, *14*, 1233156. doi:10.3389/fphar.2023.1233156.
388. Hikiami H, Goto H, Sekiya N, Hattori N, Sakakibara I, Shimada Y, et al. Comparative efficacy of Keishi-bukuryo-gan and pentoxifylline on RBC deformability in patients with “oketsu” syndrome. *Phytomedicine* **2003**, *10*, 459–466. doi:10.1078/094471103322331395.
389. Tomita T, Hirayama A, Matsui H, Aoyagi K. Effect of Keishibukuryogan, a Japanese traditional Kampo prescription, on improvement of microcirculation and Oketsu and induction of endothelial nitric oxide: A live imaging study. *Evid. Based Complement. Altern. Med.* **2017**, *2017*, 3620130. doi:10.1155/2017/3620130.
390. Brzezińska OE, Rychlicki-Kicior KA, Makowska JS. Automatic assessment of nailfold capillaroscopy software: A pilot study. *Reumatologia* **2024**, *62*, 346–350. doi:10.5114/reum/194040.
391. Karbalaie A, Etehadtavakol M, Abtahi F, Fatemi A, Emrani Z, Erlandsson BE. Image enhancement effect on inter and intra-observer reliability of nailfold capillary assessment. *Microvasc. Res.* **2018**, *120*, 100–110. doi:10.1016/j.mvr.2018.06.005.
392. Dinsdale G, Moore T, O’Leary N, Tresadern P, Berks M, Roberts C, et al. Intra-and inter-observer reliability of nailfold videocapillaroscopy—A possible outcome measure for systemic sclerosis-related microangiopathy. *Microvasc. Res.* **2017**, *112*, 1–6. doi:10.1016/j.mvr.2017.02.001.
393. Gracia Tello B, Ramos Ibáñez E, Fanlo Mateo P, Sáez Comet L, Martínez Robles E, Ríos Blanco JJ, et al. The challenge of comprehensive nailfold videocapillaroscopy practice: a further contribution. *Clin. Exp. Rheumatol.* **2022**, *40*, 1926–1932. doi:10.55563/clinexprheumatol/6usce8.
394. Helmy M, Truong TT, Jul E, Ferreira P. Deep learning and computer vision techniques for microcirculation analysis: A review. *Patterns* **2023**, *4*, 100641. doi:10.1016/j.patter.2022.100641.
395. Smith V, Pizzorni C, De Keyser F, Decuman S, Van Praet JT, Deschepper E, et al. Reliability of the qualitative and semiquantitative nailfold videocapillaroscopy assessment in a systemic sclerosis cohort: A two-centre study. *Ann. Rheum. Dis.*

- 2010**, *69*, 1092–1096. doi:10.1136/ard.2009.115568.
396. Smith V, Beeckman S, Herrick AL, Decuman S, Deschepper E, De Keyser F, et al. An EULAR study group pilot study on reliability of simple capillaroscopic definitions to describe capillary morphology in rheumatic diseases. *Rheumatology* **2016**, *55*, 883–890. doi:10.1093/rheumatology/kev441.
 397. Kornaev AV, Dremine VV, Kornaeva EP, Volkov MV. Application of deep convolutional and long short-term memory neural networks to red blood cells motion detection and velocity approximation. *Proc. SPIE* **2022**, *12194*, 1605–7422. doi:10.1117/12.2626040.
 398. Bharathi PG, Berks M, Dinsdale G, Murray A, Manning J, Wilkinson S, et al. A deep learning system for quantitative assessment of microvascular abnormalities in nailfold capillary images. *Rheumatology* **2023**, *62*, 2325–2329. doi:10.1093/rheumatology/kead026.
 399. Gracia Tello BC, Ramos Ibañez E, Saez Comet L, Guillen Del Castillo A, Simeón Aznar CP, Selva-O'Callaghan A, et al. External clinical validation of automated software to identify structural abnormalities and microhaemorrhages in nailfold videocapillaroscopy images. *Clin. Exp. Rheumatol.* **2023**, *41*, 1605–1611. doi:10.55563/clinexprheumatol/m6obl3.
 400. Emam OS, Ebadi Jalal M, Garcia-Zapirain B, Elmaghraby AS. Artificial intelligence algorithms in nailfold capillaroscopy image analysis: a systematic review. *medRxiv* **2024**, 2024-07. doi:10.1101/2024.07.28.24311154.
 401. Kassani PH, Ehwerhemuepha L, Martin-King C, Kassab R, Gibbs E, Morgan G, et al. Artificial intelligence for nailfold capillaroscopy analyses—a proof of concept application in juvenile dermatomyositis. *Pediatr. Res.* **2024**, *95*, 981–987. doi:10.1038/s41390-023-02894-7.
 402. Tuncer SA, Yildirim M, Tuncer T, Mulayim MK. YOLOv8-based system for nail capillary detection on a single-board computer. *Diagnostics* **2024**, *14*, 1843. doi:10.3390/diagnostics14171843.
 403. Ebadi Jalal M, Emam OS, Castillo-Olea C, Garcia-Zapirain B, Elmaghraby A. Abnormality detection in nailfold capillary images using deep learning with EfficientNet and cascade transfer learning. *Sci. Rep.* **2025**, *15*, 2068. doi:10.1038/s41598-025-85277-8.
 404. Ozturk L, Laclau C, Boulon C, Mangin M, Braz-Ma E, Constans J, et al. Analysis of nailfold capillaroscopy images with artificial intelligence: Data from literature and performance of machine learning and deep learning from images acquired in the SCLEROCAP study. *Microvasc. Res.* **2025**, *157*, 104753. doi:10.1016/j.mvr.2024.104753.
 405. Takimoto B, Bito K, Hari S, Taguchi H, Haneishi H. Observation and density estimation of a large number of skin capillaries using wide-field portable video capillaroscopy and semantic segmentation. *J. Biomed. Opt.* **2023**, *28*, 106003. doi:10.1117/1.JBO.28.10.106003.
 406. Li X, Cen M, Xu J, Zhang H, Xu XS. Improving feature extraction from histopathological images through a fine-tuning ImageNet model. *J. Pathol. Inform.* **2022**, *13*, 100115. doi:10.1016/j.jpi.2022.100115.
 407. Chawla S, Nakov P, Ali A, Hall W, Khalil I, Ma X, et al. Ten years after ImageNet: A 360 degrees perspective on artificial intelligence. *R. Soc. Open Sci.* **2023**, *10*, 221414. doi:10.1098/rsos.221414.
 408. Deng J, Dong W, Socher R, Li L-J, Li K, Li F-F. ImageNet: A large-scale hierarchical image database. In Proceedings of the 2009 IEEE Conference on Computer Vision and Pattern Recognition, Miami, FL, USA, 20–25 June 2009; pp. 248–255. doi:10.1109/CVPR.2009.5206848.
 409. Kim S, Chen J, Cheng T, Gindulyte A, He J, He S, et al. PubChem 2025 update. *Nucleic Acids Res.* **2025**, *53*, D1516–D1525. doi:10.1093/nar/gkae1059.
 410. Fleming J, Magana P, Nair S, Tsenkov M, Bertoni D, Pidruchna I, et al. AlphaFold Protein Structure Database and 3D-Beacons: New Data and Capabilities. *J. Mol. Biol.* **2025**, *437*, 168967. doi:10.1016/j.jmb.2025.168967.
 411. Varadi M, Bertoni D, Magana P, Paramval U, Pidruchna I, Radhakrishnan M, et al. AlphaFold Protein Structure Database in 2024: Providing structure coverage for over 214 million protein sequences. *Nucleic Acids Res.* **2024**, *52*, D368–D375. doi:10.1093/nar/gkad1011.
 412. Berman HM, Burley SK. Protein Data Bank (PDB): Fifty-three years young and having a transformative impact on science and society. *Q. Rev. Biophys.* **2025**, *58*, e9. doi:10.1017/S0033583525000034.
 413. Holzinger A, Biemann C, Pattichis CS, Kell DB. What do we need to build explainable AI systems for the medical domain? *arXiv* **2017**, arXiv:1712.09923.
 414. Arron HE, Marsh BD, Kell DB, Khan MA, Jaeger BR, Pretorius E. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: The biology of a neglected disease. *Front. Immunol.* **2024**, *15*, 1386607. doi:10.3389/fimmu.2024.1386607.
 415. Legler F, Meyer-Arndt L, Modl L, Kedor C, Freitag H, Stein E, et al. Long-term symptom severity and clinical biomarkers in post-COVID-19/chronic fatigue syndrome: results from a prospective observational cohort. *EClinicalMedicine* **2023**, *63*, 102146. doi:10.1016/j.eclinm.2023.102146.
 416. van Campen CLMC, Rowe PC, Visser FC. Orthostatic Symptoms and Reductions in Cerebral Blood Flow in Long-Haul COVID-19 Patients: Similarities with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Medicina* **2021**, *58*, 28. doi:10.3390/medicina58010028.
 417. Haffke M, Freitag H, Rudolf G, Seifert M, Doehner W, Scherbakov N, et al. Endothelial dysfunction and altered endothelial biomarkers in patients with post-COVID-19 syndrome and chronic fatigue syndrome (ME/CFS). *J. Transl. Med.* **2022**, *20*,

138. doi:10.1186/s12967-022-03346-2.
418. Newton DJ, Kennedy G, Chan KK, Lang CC, Belch JJ, Khan F. Large and small artery endothelial dysfunction in chronic fatigue syndrome. *Int. J. Cardiol.* **2012**, *154*, 335–336. doi:10.1016/j.ijcard.2011.10.030.
419. Nunes JM, Kell DB, Pretorius E. Herpesvirus Infection of Endothelial Cells as a Systemic Pathological Axis in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Viruses* **2024**, *16*, 572. doi:10.3390/v16040572.
420. Nunes JM, Vlok M, Proal A, Kell DB, Pretorius E. Data-independent LC-MS/MS analysis of ME/CFS plasma reveals a dysregulated coagulation system, endothelial dysfunction, downregulation of complement machinery. *Cardiovasc. Diabetol.* **2024**, *23*, 254. doi:10.1186/s12933-024-02315-x.
421. McLaughlin M, Sanal-Hayes NEM, Hayes LD, Berry EC, Sculthorpe NF. People With Long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) Exhibit Similarly Impaired Vascular Function. *Am. J. Med.* **2023**, *138*, 530–566. doi:10.1016/j.amjmed.2023.09.013.
422. Wirth KJ, Löhn M. Microvascular Capillary and Precapillary Cardiovascular Disturbances Strongly Interact to Severely Affect Tissue Perfusion and Mitochondrial Function in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Evolving from the Post COVID-19 Syndrome. *Medicina* **2024**, *60*, 194. doi:10.3390/medicina60020194.
423. Vaes AW, De Boever P, Franssen FME, Uszko-Lencer N, Vanfleteren L, Spruit MA. Endothelial function in patients with COPD: An updated systematic review of studies using flow-mediated dilatation. *Expert. Rev. Respir. Med.* **2023**, *17*, 53–69. doi:10.1080/17476348.2023.2176845.
424. Garcia DJ, Chagnot A, Wardlaw JM, Montagne A. A Scoping Review on Biomarkers of Endothelial Dysfunction in Small Vessel Disease: Molecular Insights from Human Studies. *Int. J. Mol. Sci.* **2023**, *24*, 13114. doi:10.3390/ijms241713114.
425. Garcia VP, Fandl HK, Wegerson KN, Berry AR, Ruzzene ST, Greiner JJ, et al. Elevated circulating endothelial cell-derived microvesicles: A biomarker of endothelial vasomotor dysfunction in adults with obesity. *J. Appl. Physiol. (1985)* **2025**, *138*, 1143–1149. doi:10.1152/japplphysiol.00081.2025.
426. Mohebbi A, Haybar H, Nakhaei Moghaddam F, Rasti Z, Vahid MA, Saki N. Biomarkers of endothelial dysfunction are associated with poor outcome in COVID-19 patients: A systematic review and meta-analysis. *Rev. Med. Virol.* **2023**, *33*, e2442. doi:10.1002/rmv.2442.
427. Zhang J. Biomarkers of endothelial activation and dysfunction in cardiovascular diseases. *Rev. Cardiovasc. Med.* **2022**, *23*, 73. doi:10.31083/j.rcm2302073.
428. Attia ABE, Moothanchery M, Li X, Yew YW, Thng STG, Dinis US, et al. Microvascular imaging and monitoring of hemodynamic changes in the skin during arterial-venous occlusion using multispectral raster-scanning optoacoustic mesoscopy. *Photoacoustics* **2021**, *22*, 100268. doi:10.1016/j.pacs.2021.100268.
429. Geisler EL, Brannen A, Pressler M, Perez J, Kane AA, Hallac RR. 3D imaging of vascular anomalies using raster-scanning optoacoustic mesoscopy. *Lasers Surg. Med.* **2022**, *54*, 1269–1277. doi:10.1002/lsm.23588.
430. Nitkunanantharajah S, Haedicke K, Moore TB, Manning JB, Dinsdale G, Berks M, et al. Three-dimensional optoacoustic imaging of nailfold capillaries in systemic sclerosis and its potential for disease differentiation using deep learning. *Sci. Rep.* **2020**, *10*, 16444. doi:10.1038/s41598-020-73319-2.
431. Böke JS, Popp J, Krafft C. Optical photothermal infrared spectroscopy with simultaneously acquired Raman spectroscopy for two-dimensional microplastic identification. *Sci. Rep.* **2022**, *12*, 18785. doi:10.1038/s41598-022-23318-2.
432. Gvazava N, Konings SC, Cepeda-Prado E, Skoryk V, Umeano CH, Dong J, et al. Label-free high-resolution photothermal optical infrared spectroscopy for spatiotemporal chemical analysis in fresh, hydrated living tissues and embryos. *J. Am. Chem. Soc.* **2023**, *145*, 24796–24808. doi:10.1021/jacs.3c08854.
433. Lima C, Ahmed S, Xu Y, Muhamadali H, Parry C, McGalliard RJ, et al. Simultaneous Raman and infrared spectroscopy: A novel combination for studying bacterial infections at the single cell level. *Chem. Sci.* **2022**, *13*, 8171–8179. doi:10.1039/d2sc02493d.
434. Lima C, Muhamadali H, Goodacre R. Monitoring Phenotype Heterogeneity at the Single-Cell Level within Bacillus Populations Producing Poly-3-hydroxybutyrate by Label-Free Super-resolution Infrared Imaging. *Anal. Chem.* **2023**, *95*, 17733–17740. doi:10.1021/acs.analchem.3c03595.
435. Richardson PIC, Horsburgh MJ, Goodacre R. Benchmarking classification abilities of novel optical photothermal IR spectroscopy at the single-cell level with bulk FTIR measurements. *Anal. Methods* **2024**, *16*, 5419–5425. doi:10.1039/d4ay00810c.
436. Davison AK, Dinsdale G, New P, Manning J, Patrick H, Taxiarchi VP, et al. Feasibility study of mobile phone photography as a possible outcome measure of systemic sclerosis-related digital lesions. *Rheumatol. Adv. Pract.* **2022**, *6*, rkac105. doi:10.1093/rap/rkac105.
437. Madenidou AV, Dinsdale G, Samaranyaka M, Muir L, Dixon WG, Herrick AL. Smartphone images of digital ulcers provide a clear picture of disease progression for the first rheumatology visit. *Rheumatology* **2023**, *62*, e153–e154. doi:10.1093/rheumatology/keac561.
438. Davison AK, Krishan A, New RP, Murray A, Dinsdale G, Manning J, et al. Development of a measuring app for systemic sclerosis-related digital ulceration (SALVE: Scleroderma App for Lesion VErification). *Rheumatology* **2024**, *63*, 3297–3305.

doi:10.1093/rheumatology/keae371.

439. Kell DB. Reviews turn facts into understanding. *Nature* **2012**, 490, 37. doi:10.1038/490037e.