Ultrasound lymph node examination of the lower extremities

Sonografische Lymphknotendiagnostik im Bereich der unteren Extremitäten

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ABSTRACT

Sonography is used to detect and characterize palpable resistance or accidentally discovered lymph nodes (LN) of the lower extremities. In most cases, these are chronically inflammatory or reactive lymph nodes without clinical relevance. They are almost always found only in the groin, while LN only occur very rarely in the popliteal. In addition to the patient's medical history and clinic, B-scan sonography and vascular architecture also play a decisive role in differential diagnosis. Due to the unspecific sonographic findings, it is not always possible to differentiate reliably between inflammatory and lymphoma diseases in a singular LN: Therefore, a thickening of the cortex with preserved vascular architecture, for example, is found in lymphomas as well as in inflammation-reactive LN. An US targeted biopsy can be diagnostically helpful. A metastatic transformation often goes hand in hand with the destruction of the LN architecture and the orderly vascular image. Also important is the LN delimitation and central ischemia in the color-coded and contrast-enhanced sonography.

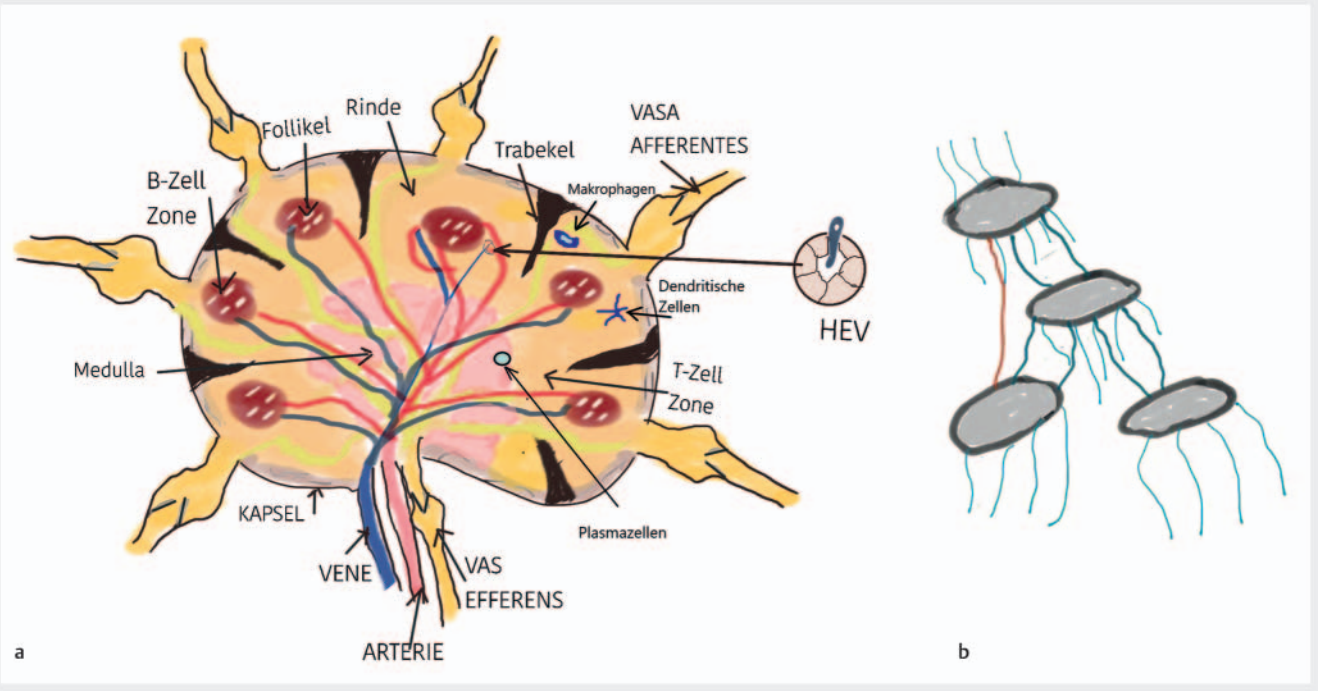
ZUSAMMENFASSUNG

Die Sonografie dient der Detektion und Charakterisierung tastbarer Resistenzen oder zufällig entdeckter Lymphknoten (LK) der unteren Extremitäten. Meist handelt es sich um chronisch entzündliche oder reaktive Lymphknoten ohne klinische Relevanz. Sie finden sich fast immer nur inguinal, während LK in der Kniekehle sehr selten auftreten. Für die Differenzialdiagnose kommt neben Anamnese und Klinik der B-Bild-Sonografie sowie der Gefäßarchitektur eine wegweisende Rolle zu. Wegen der unspezifischen sonografischen Befunde kann bei einem singulären LK nicht sicher zwischen entzündlichen und Lymphomerkrankungen unterschieden werden: So findet sich eine Rindenverdickung bei erhaltener Gefäßarchitektur sowohl bei Lymphomen als auch bei entzündlich-reaktiven LK. Eine US-gezielte Biopsie kann diagnostisch wegweisend sein. Eine metastatische Transformation geht sonografisch oft mit einer Zerstörung der LK-Architektur und des geordneten Gefäßbildes einher. Wichtig sind ferner die LK-Abgrenzbarkeit und die zentrale Ischämie in der farbkodierten und kontrastverstärkten Sonografie.

Introduction, functional anatomy

It is estimated that the tissues produce about two litres of lymph in 24 hours. This fluid is transported together with immunocompetent cells via the open ends of the lymphatic vessels to reach the nearest lymph node (LN). The lymph vessels have a delicate valve system and run parallel to the blood vessels. The lymph flows through several afferent lymphatics into the functional compartments of the LN, which are divided by septa. As the lymph passes through the lymph node, antigens recognised as foreign are filtered out (▶ **Fig. 1a**). The lymph so 'cleaned' continues proximally via one or more efferent lymphatic vessels (▶ **Fig. 1b**). After passing through further LNs, it reaches the abdominal and thoracic lymphatics, from where it is eventually returned to the central venous system [1].

Of an estimated 300–700 lymph nodes in the body, about one-third are found in the neck region (frequent portal of entry for many pathogens). Ultrasound scanning can therefore always detect LNs in the neck. Lymph nodes can also be found in the groin



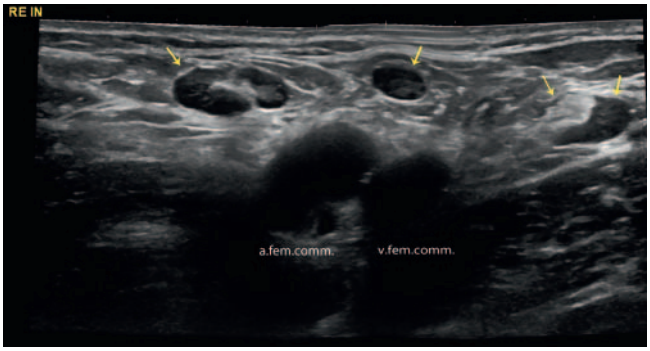
▶ **Fig. 1** **a** Simplified diagram of a lymph node structure. The inflowing lymph is divided into several compartments (the spaces between two trabeculae) After being filtered, the fluid drains through one or more efferent lymphatics. Follicles (B cells) are found in the outer cortical layer and the T lymphocytes in the inner layer. The blood supply is situated in the hilum. At the end of the arterial and venous systems, are the high endothelial venules (HEVs), through which immunocompetent cells from the blood vessels enter the lymph node tissue. In the node, antigens are captured by dendritic cells and presented to the activated lymphocytes for cellular and humoral elimination. **b** Lymphography image of the afferent and efferent lymphatics [2].

of almost every person, as long as an appropriate transducer is used.

An intact lymph node consists of cortex, medulla and hilar region and is enveloped by a capsule. High frequency transducers may occasionally reveal small hypoechoic follicles in inflamed or lymphomatous LNs (▶ **Fig. 3**). Blood vessels supplying the node are found in the hilum, together with the draining (efferent) lymphatic vessel.

Ultrasound tools and examination

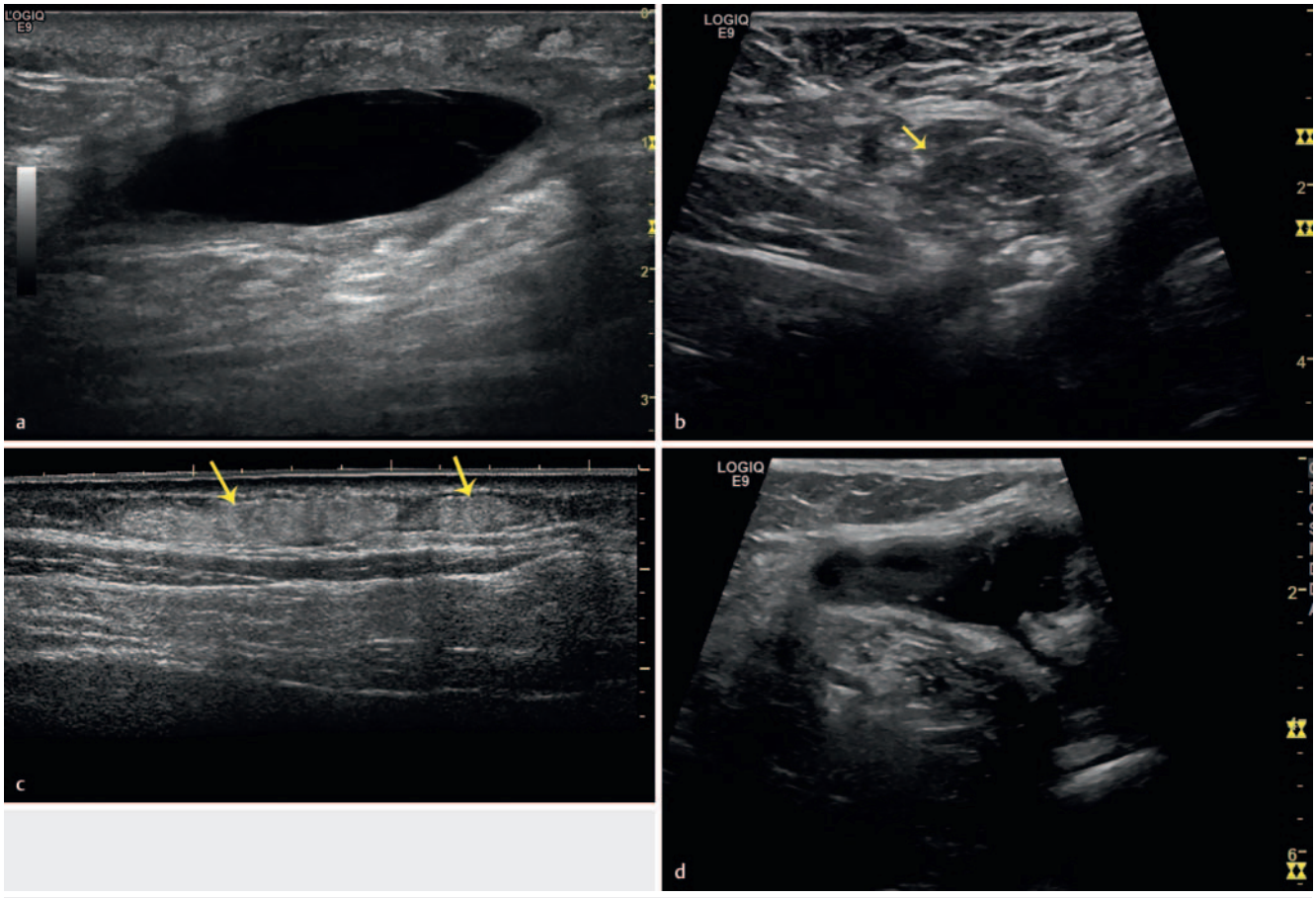
As a rule, linear transducers of between 7.5 and 20 MHz are used in the periphery: the shallower the LN lies, the higher the selected transducer frequency should be. Besides B-mode scans, colour-coded Doppler ultrasound is used regularly and a few companies have even patented flow-detection procedures such as B-Flow (demonstration of flowing blood as shining white points by discriminating stationary echoes from moving echoes) and Superb Microvascular Imaging (SMI) with artefact-reducing duplex ultrasound [3–5]. Elastography and contrast-enhanced ultrasound (CEUS), as shown in ▶ **Fig. 4b**, are only used in exceptional circumstances [6]. If necessary, a C-plane (panoramic image) can be generated from a frozen tissue block, whereupon the sectional plane is then parallel to the cutis (▶ **Fig. 2, 6b**). Ultrasonography is also used to guide fine needle aspiration (FNA) or core needle biopsy, often obtaining a firm diagnosis. Open resection of a lymph node



▶ **Fig. 2** Horizontally lying lymph nodes transformed by non-Hodgkin lymphoma (yellow arrows). The LN on the left shows a clearly thickened cortex, the one in the middle does not have a recognisable echogenic centre, the LN on the right still has a thin cortex while the medial part is clearly hypoechoic and thickened. The femoral vessels lie posteriorly and can be seen in oblique section.

is particularly recommended for the definitive typing of lymphomas. The AWMF guidelines do not recommend the elective surgical removal of the sentinel lymph node [7, 8] (▶ **Table 1**).

The examination is initially performed along the inguinal ligament and proximal large vessels in transverse section, using an anatomically suitable high frequency linear transducer (probe). If a LN is detected, it must be measured in two planes. The ratio between the longitudinal and transverse diameters (Solbiati or Vassallo Index) may be of limited use in the differential diagnosis



▶ **Fig. 3** **a** Postoperative seroma with surrounding oedema in the groin. **b** Baker's cyst (knee joint). **c** Inguinal hernia (arrow) after Valsalva manoeuvre. **d** Palpable subcutaneous lipoma, without any vascularisation to be seen on colour Doppler (arrows).

of metastatic disease (▶ **Table 2**): if the ratio is less than 2, metastasis must be confirmed or ruled out [9, 10]. Elongated LNs with a Solbiati Index > 2 are less specific with respect to whether they are benign or malignant. A sweep in both ultrasound axes is then performed. In B-mode, attention must be paid to a clear demarcation from the surrounding tissues. With a sensitive flow detection procedure, colour Doppler can be used to show the vascularisation of the node, while CEUS shows the tissue perfusion [6, 11]. These procedures also serve to demonstrate the vascular structure. The role of the imaging is therefore to detect and localise LNs, to establish their characteristics and to assist with the biopsy, if necessary. CEUS can deliver additional information, but requires an experienced examiner and is reserved for specific situations [5]. The value of elastography in the differential diagnosis has not yet been conclusively clarified.

Localisation, common differential diagnoses

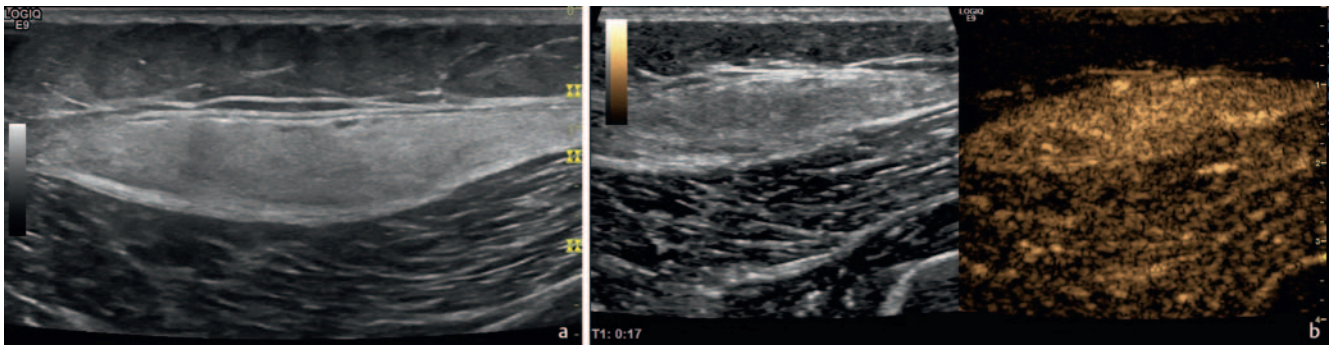
A distinction is made between superficial horizontal (lying laterally and medially immediately below the inguinal ligament), supero-lateral, and supero-medial LNs (▶ **Fig. 2**). In contrast to the deeper-lying nodes, these superficial LNs can often be palpated. The superficial inferior LNs lie somewhat inferior to the saphenous opening (saphenous hiatus). The deeper-lying LNs are in the subfascial tissues medial to the femoral vessels (see Brenner in this issue). Important clinical parameters are the LN size and tenderness. Unlike chronically inflamed or reactive LNs, acutely inflamed nodes are usually palpable or tender to touch and cause patients to visit their doctors.

Lymph nodes in the popliteal fossa are very rare and, as a rule, of inflammatory or cancerous origin [12]. They are usually a result of distal inflammation or infection (e. g. erysipelas, venous leg ulcers) or cutaneous malignancies [13].

Lymph drains from the legs, external genitalia and the buttocks drains via the inguinal LNs as does lymph from the skin and subcutaneous tissues below the umbilicus.

Local differential diagnoses frequently include lipmas, hernias, joint effusions, postoperative seromas and haematomas (▶ **Fig. 3a–d, 4a, b**).

Focal echogenic lesions, usually lying in the subcutaneous tissue, are most likely to be consistent with palpable lipomas (▶ **Fig. 3 d, 4a, b**). Colour Doppler scans reveal no vascularisation. Histological examination must be performed, if there is growth or evidence of intralesional vessels [14].



▶ **Fig. 4** **a** Palpable mass on the inner aspect of the thigh on the adductor longus muscle corresponds to a clearly demarcated echogenic spindle-shaped lipoma measuring 53 mm × 9 mm. **b** Surgical resection was performed because of the clearly visible vascularisation seen on colour Doppler and the hyperperfusion in the contrast enhanced ultrasound (CEUS).

▶ **Table 1** Technical ultrasound scanning procedures.

Technique, assessment criteria			
Choice of transducer	Linear transducer, the more superficial the LN, the higher the frequency; the frequency for colour coding is lower than in the underlying B-mode image Display modes: C-plane, extended field of view		
B-mode: Fundamental, tissue harmonic imaging (THI)	Number, difference between sides, local tenderness to pressure, distance from the primary tumour	LN structure: cortex/medulla/hilum	Capsule intact, local oedema?
Colour Doppler: Power Doppler, B-Flow, SMI	Intranodal vessels? Vascular structure	Demonstration of arteries & veins	Perinodal vessels
Elastography (strain and shear wave elastography)	Colour-coded representation of local tissue firmness	Strain elastography Please note: only comparative values are shown	Shear wave elastography: absolute local values are given in m/s or kPa
CEUS	Direction of contrast enhancement: centripetal, centrifugal	Homogeneous/absent enhancement?	Perinodal contrast enhancement?

Inflammatory/Reactive lymph nodes

Inguinal lymph nodes, which are usually of chronic inflammatory or reactive origin, are found in nearly everyone. The cortex may be extremely narrow (< 1 mm) and there is usually no vascularisation to be seen on colour Doppler. The centre of the LN usually shows echogenicity (adipose tissue, see ▶ **Fig. 5b, 6a–d**), but in some instances may be less echogenic than the fatty tissue surrounding the node (▶ **Fig. 5b**).

The thickness of the cortex (follicles, paracortex) and the degree of vascularisation increase with the inflammatory activity (▶ **Fig. 5a–d, 6c–e, 7a–c, 8**). Regional cortical expansion can be seen, if the afferent lymphatic vessels drain antigens into the responsible LN compartments (▶ **Fig. 1, 6a–e**) and thus trigger a regional immune response. Acutely inflamed LNs are usually unilateral.

Benign lymphadenopathy is often self-limiting.

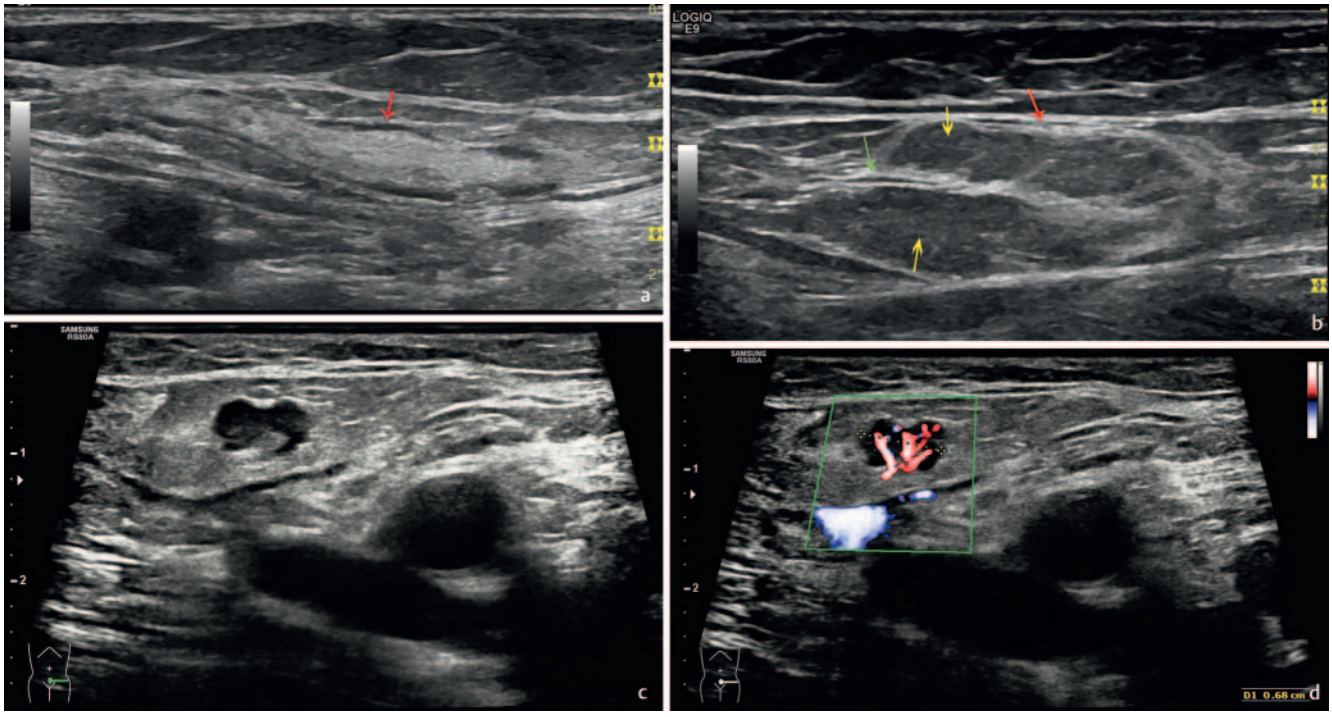
With respect to the aetiology, autoimmune diseases (e. g. rheumatoid arthritis, dermatomyositis, lupus erythematosus), pharmacotherapy (e. g. interferon therapy), and iatrogenic causes (e. g. local interventions) come into question besides acute and chronic inflammation and infections of the skin such as psoriasis and atopic eczema (▶ **Fig. 8a–f**) [14, 15].

▶ **Table 2** gives the most important ultrasound criteria for distinguishing between inflammatory/reactive nodes, metastatic disease and nodal lymphoma. The size of the nodes alone is not a differentiating characteristic.

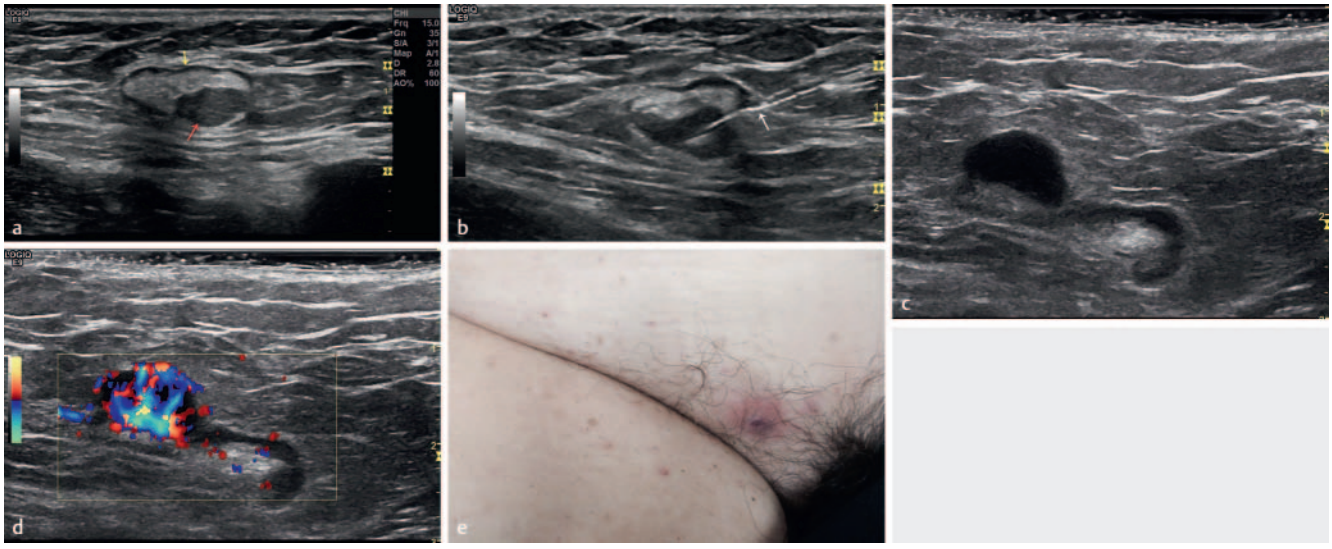
Abscess formation in inflamed LNs is rare and usually found in the neck (e. g. tuberculosis) or in the groin in the case of venereal diseases or immune incompetence.

Lymph nodes transformed by metastasis

Ultrasound scanning is clearly superior to palpation in the detection of lymph node metastases [16]. Malignant infiltration of lymph nodes in the lower limb is most often due to malignant melanoma, malignant lymphomas, squamous cell carcinoma of the anal canal, vulva and penis, sarcomas and cutaneous squamous cell carcinomas, also of the trunk. As the tumour cells usually grow concentrically from the edge or centre of the node, lymphatic metastases usually appear as asymmetrical hypoechoic

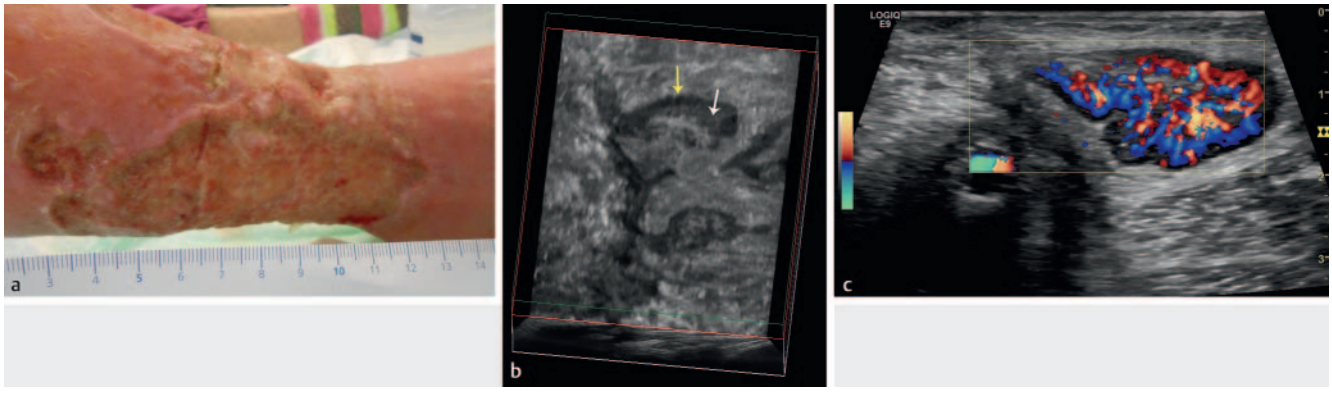


▶ **Fig. 5** **a** Central echogenic (adipose), elongated LN with a cortex measuring approx. 0.7 mm (red arrow). **b** Central less echogenic medulla (yellow arrows: fatty infiltrate); narrow cortex measuring approx. 0.6 mm (red arrow). **c, d** LN measuring 7 mm with thickened cortex that is hypoechoic relative to the echogenic hilum. **b** Regular vascular arrangement in the colour Doppler.

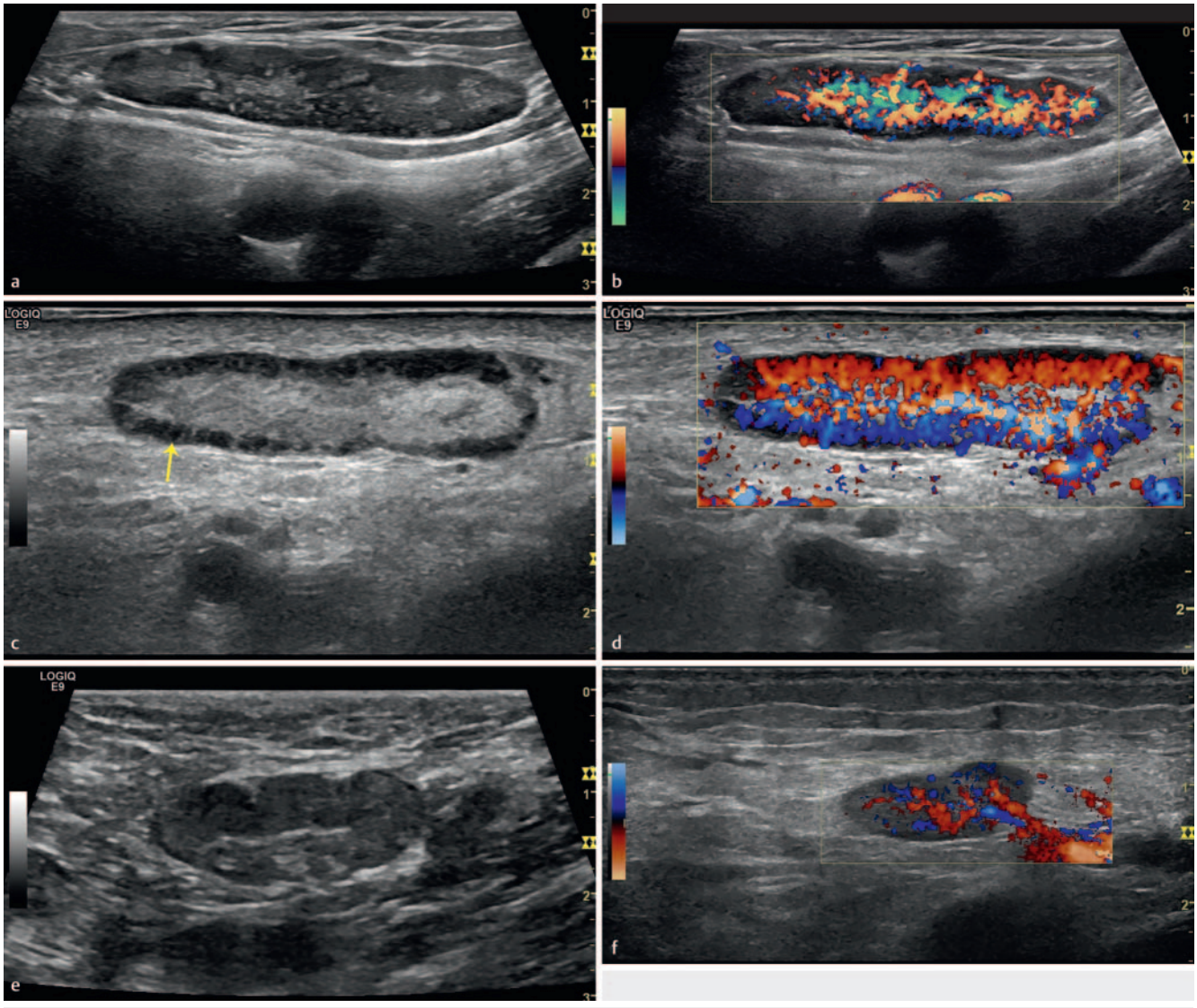


▶ **Fig. 6** **a** Regional adipose area (red arrow), narrow cortex (yellow arrow). **b** Reflection from the needle (white arrow) used for cytological confirmation. **c, d** Regional hypoechoic thickened segment of cortex, seen on colour Doppler to be hypervascularised with a regular vascular arrangement. **e** Cause: hair follicle inflammation.

cortical nodules or rounded hypoechoic lymph node lesions. With haematogenous spread, tumours may initially be confined to the centre of the node, sparing the cortical region. In contrast to inflammatory and sometimes lymphomatous changes in the LNs, the nodes are often spherical: the ratio between the maximum longitudinal measurement and the maximum transverse measurement is usually between 1 and < 2 [9, 10]. A further important criterion concerns tumour vascularisation and perfusion. Tumour blood vessels do not have a muscular layer and show pores of varying size in their walls. Fluid can therefore be squeezed out of the vascular lumen into the LN tumour tissue. This leads to an increase in the interstitial pressure and thus to a reduction in tissue perfusion. The middle of the tumour becomes ischaemic and eventually necrotic [17, 18]. If the capsule is damaged by



▶ **Fig. 7** **a** Chronic lower leg ulcer, almost circumferential. **b** C-plane* demonstrating one of several LNs with follicles (yellow arrow); paracortex (white arrow). **c** Colour Doppler shows considerable hypervascularisation with normal vascular arrangement (tree-like branching arteries and veins). *C-plane: B-mode reconstruction parallel to the skin from one sweep.

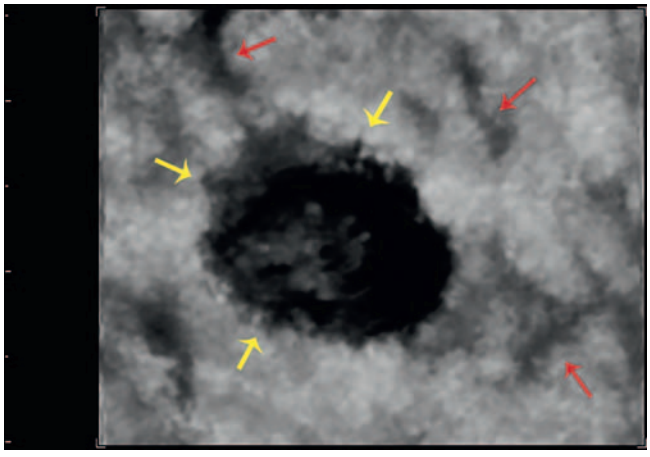


▶ **Fig. 8** Female patient with melanoma on interferon therapy. **a** Elongated inguinal LN with thickened cortex, Solbiati Index > 2 and **b** increased arterial and venous vascularisation with normal vascular structure. Reactive LN confirmed on histology. **c** Inguinal LN with hypertrophied follicles (arrow), Solbiati Index > 2. **d** Hypervascularised LN with regular arterial vascular structure. **e** Patient with psoriasis, showing thickened cortex, Solbiati Index approx. 2, and **f** regular vascular arrangement at the hilum.

▶ **Table 2** General assessment criteria for lymph nodes. Characteristics in inflammatory/reactive, lymphomatous and metastatically transformed lymph nodes.

Ultrasound tumour characteristics			
Mode	**Inflammatory/Reactive Lymph Nodes**		
B-mode	Acute inflammation: usually evenly thickened cortex, hypoechoic medulla. Usually elongated (LD/TD > 2). Number and size decrease with distance from cause.	Chronic inflammation: evenly narrow cortex, echogenic centre	Acute: rarely perinodal streaky fluid (oedema)
Colour Doppler	Regional/global hyper-vascularisation, regressing as becomes chronic	Evidence of arteries and veins	Tree-like branching vascular structure
CEUS	Clear centrifugal homogeneous hyperperfusion (acute inflammation)	Little perfusion with chronic inflammation	Usually no evidence of perinodal perfusion
	Lymphoma		
B-mode	As inflammatory, sometimes pattern of small nodules in the perinodal thickened cortex (follicles), no echogenic hilum	Multiple, usually bilateral, more peripheral LN stations affected	Usually no perinodal oedema; abdominal involvement (LNs and/or organs)
Colour Doppler	Hypervascularisation	Usually evidence of arteries and veins	Tree-like branching vascular structure
CEUS	Clear centrifugal homogeneous hyperperfusion	Possibly peripheral hypoperfusion	Usually no perinodal oedema
	Carcinoma/sarcoma metastases		
B-mode	Nodular thickening or spherical shape (LD/TD < 2) (route of spread?)	Rounded hypoechoic cystic LN, no echogenic hilum	Perinodal oedema with capsular infiltration
Colour Doppler	Slight to strong vascularisation, central vessels sometimes absent, supply via capsular arteries	Usually chaotic vascular structure	Usually no perinodal vascularisation
CEUS	Slight to strong centripetal perfusion	Inhomogeneous perfusion, central ischaemia/necrosis	Perinodal contrast enhancement (with infiltration through the capsule)

LD: Longitudinal diameter, TD: Transverse diameter, CEUS: Contrast enhanced ultrasound.



▶ **Fig. 9** Fine spicules of hypoechoic extension beyond the LN capsule (yellow arrows) indicate tumour invasion, usually with accompanying regional oedema (red arrows).

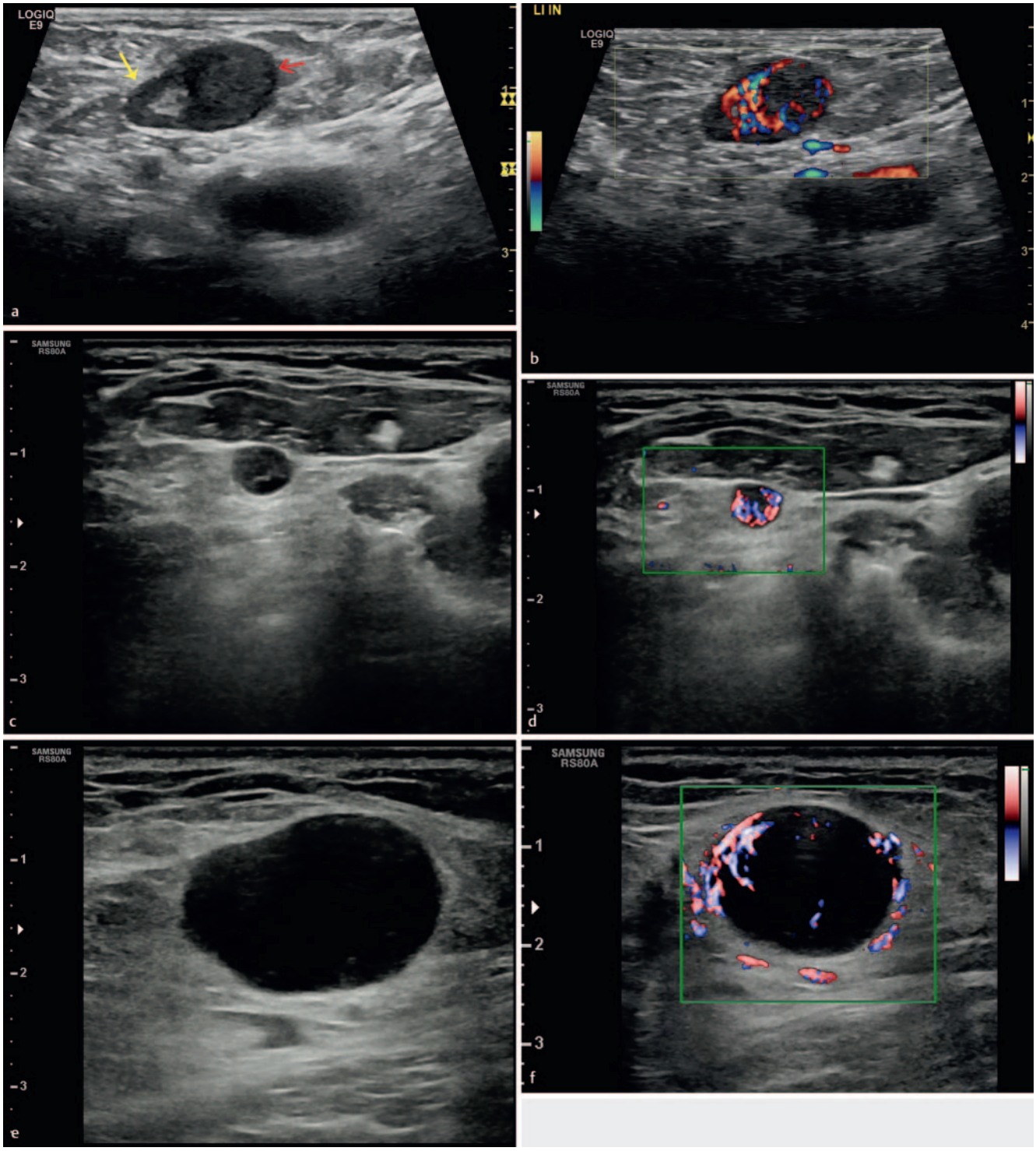
tumour invasion, fluid can leak out of the lymph tissue and lead to a perinodal oedema (▶ **Fig. 9**).

The nutritional and O_2 requirements are ensured not only by the hilar arterial branches but – especially when there is central ischaemia or necrosis – also by capsular arteries radiating into the LN (▶ **Fig. 10a–f, 11a, b, 12a, b**).

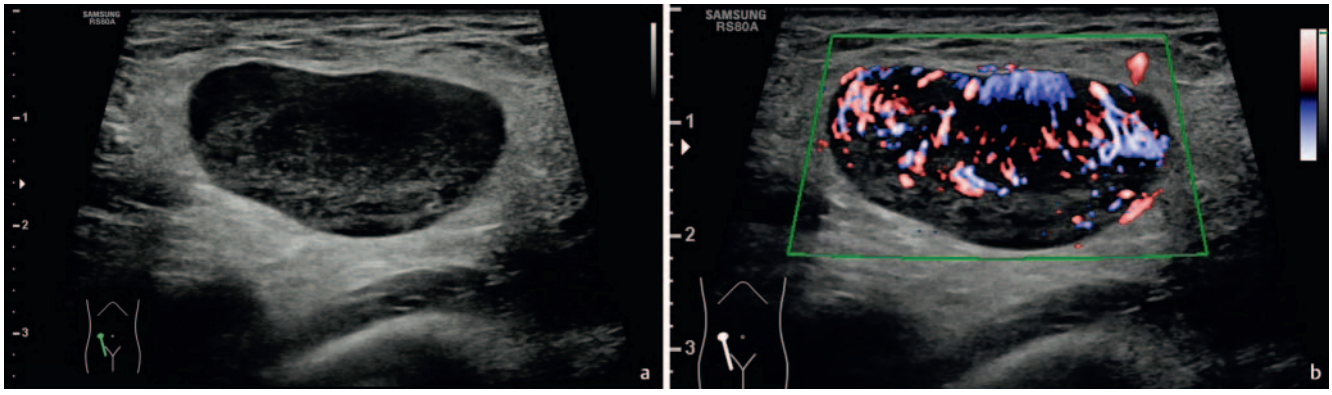
Lymphomas

When possibly malignant inguinal lymph nodes are an incidental finding, it must be decided whether they are a manifestation of systemic disease or a regional LN metastasis. Clinical data are decisive. In children and adolescents, an inflammatory/reactive aetiology is most likely. Fine needle aspiration (FNA) to confirm the diagnosis is recommended by some authors [19].

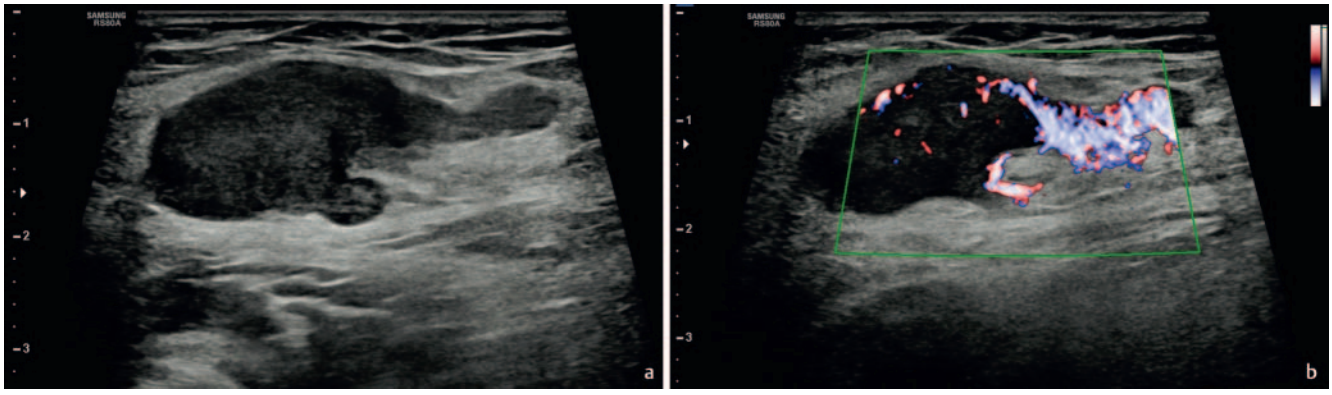
Isolated inguinal Hodgkin lymphoma (stage 1) tends to be rare and appears as a hypoechoic or cystic cortical enlargement in the B-mode scan. In the case of non-Hodgkin lymphoma, suspicious LNs are usually found at several LN stations; abdominal manifestations (lymph nodes, involvement of the spleen or liver) are also



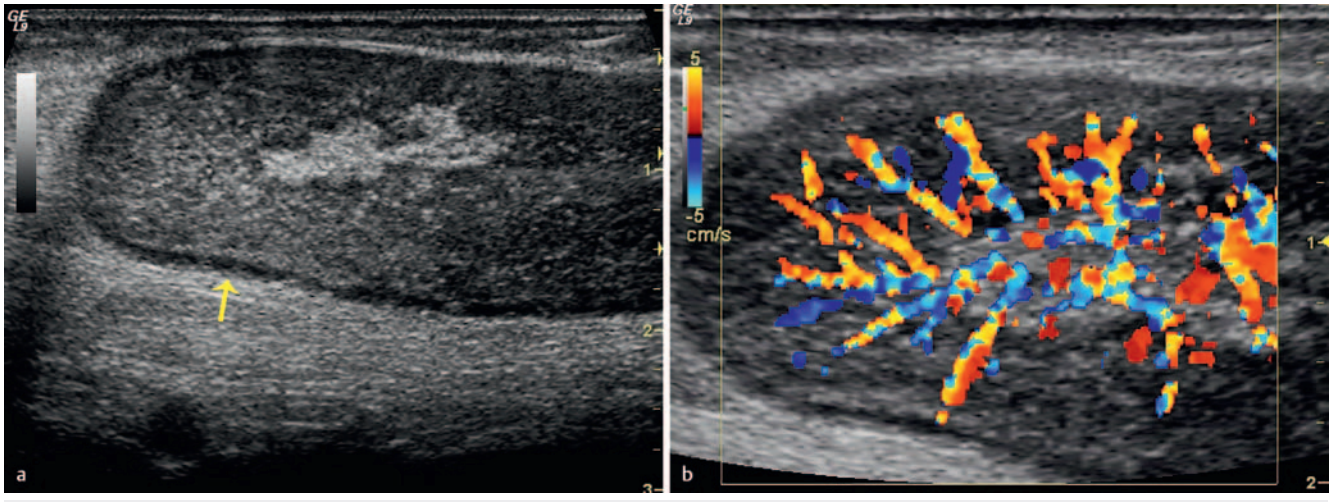
▶ **Fig. 10** **a** Inguinal metastases from a sarcoma (yellow arrow: normal LN cortex; red arrow: round metastasis, about 1 cm in size). **b** Tumour vessels entering from the periphery, ischemic tumour centre. **c** 5 mm spherical hypoechoic inhomogeneous metastasis from a melanoma, completely infiltrating the LN with **d** vessels entering from the periphery. **e** Spherical melanoma metastasis appearing almost cystic and completely infiltrating the LN with **f** central ischaemia and peripheral vascular supply via capsular arteries, central ischaemia.



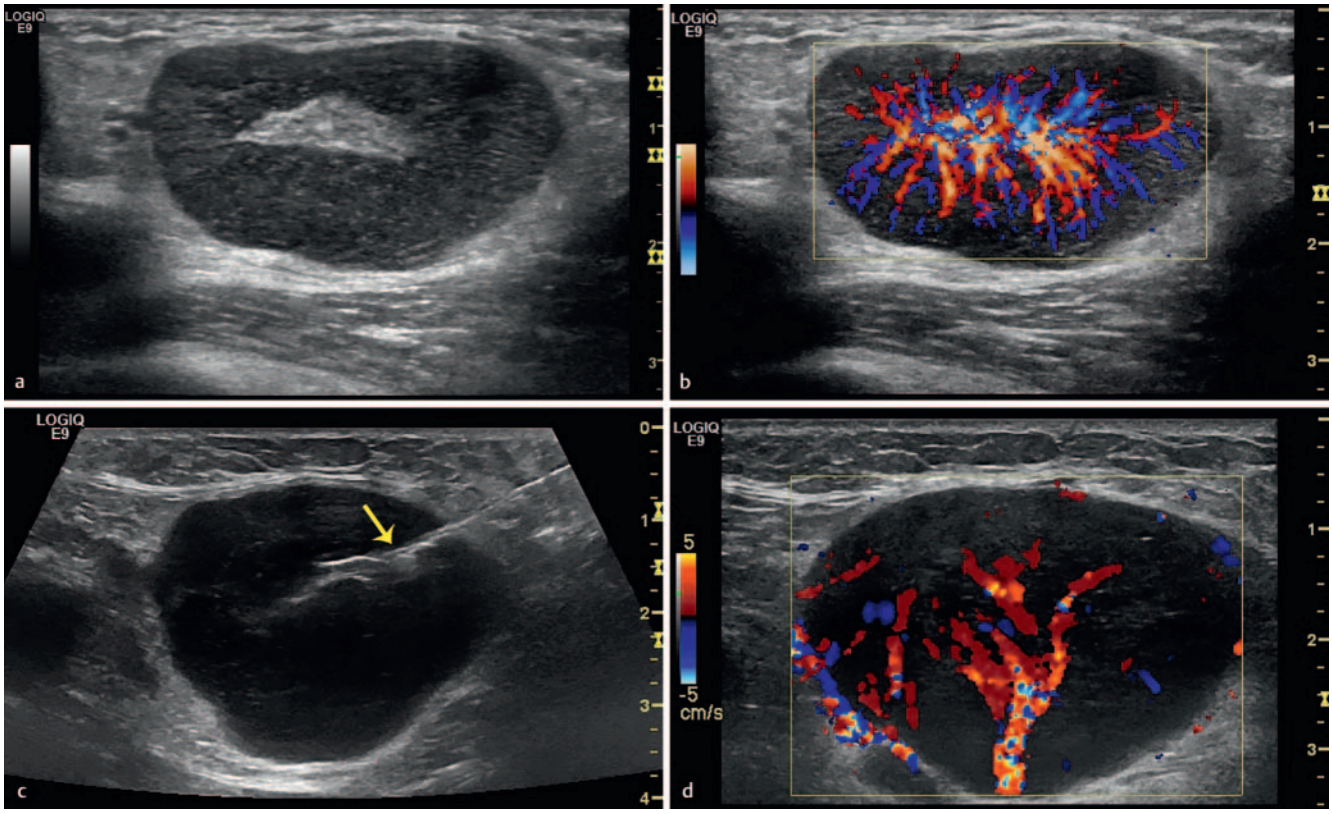
▶ **Fig. 11** Hypervascularised inguinal melanoma metastasis. Solbiati Index < 2. **a** B-mode image of the hypoechoic cortex and hypoechoic medulla with central tumour infiltration. **b** Colour Doppler shows an additional vascular supply via the capsular arteries.



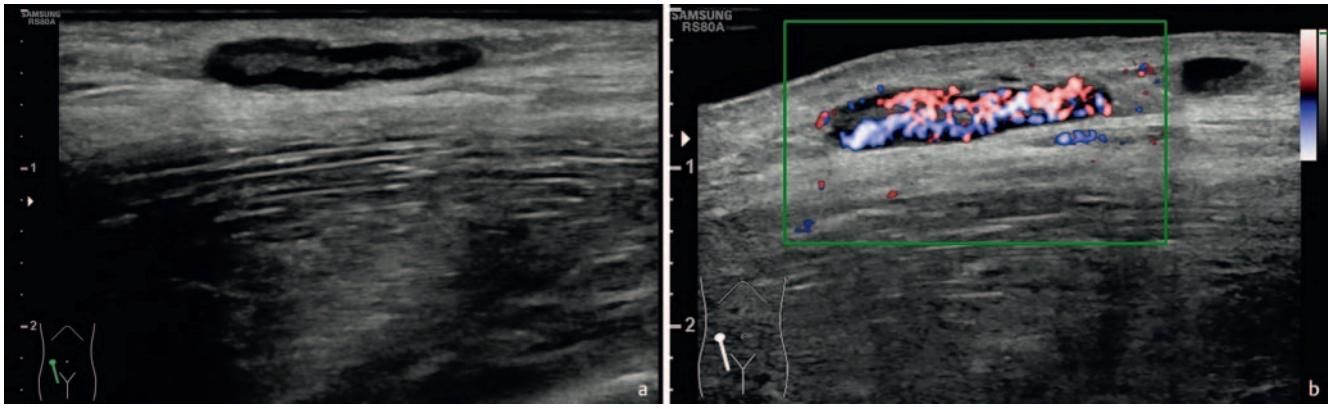
▶ **Fig. 12** Situation after minimally invasive surgery for cervical cancer. Four months later, there was an inguinal LN metastasis. **a** Enlargement of the proximal end of the LN (left in the picture), showing **b** only minimal peripheral vascularisation, while the still intact inferior cortex is clearly hypervascular.



▶ **Fig. 13** B cell non-Hodgkin lymphoma (B-NHL). **a** In the B-mode scan, multiple fine nodules can be seen in the medulla in addition to a thin hypoechoic cortex (arrow). **b** Colour Doppler shows increased vascularisation with a preserved vascular structure.



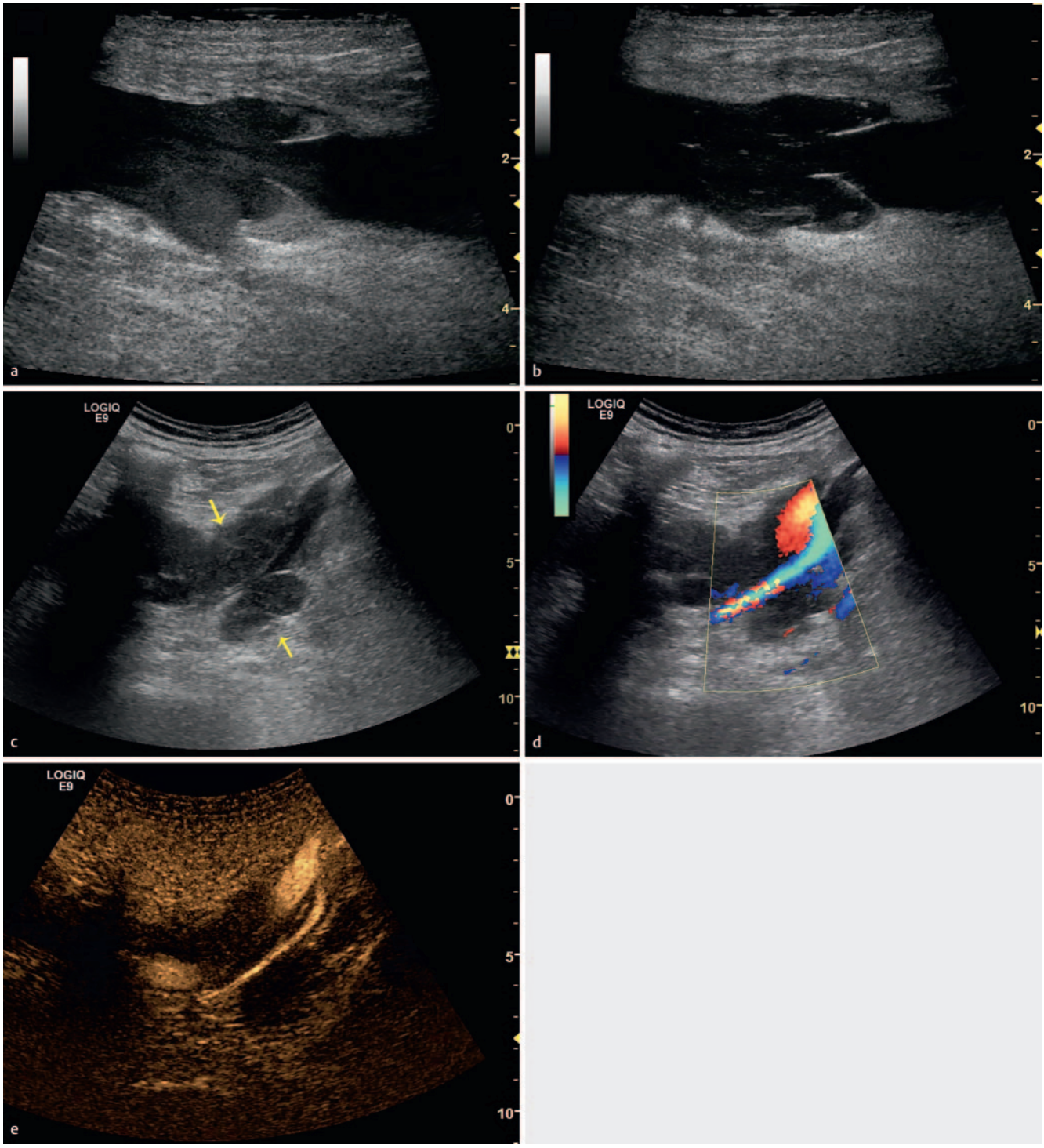
▶ **Fig. 14** Typical peripheral lymph nodes in B-NHL, all with a Solbiati Index < 2. **a** In the B-mode scan, hypoechoic cortical thickening with small hypoechoic nodules and still intact echogenic centre. **b** Hypervascularised LN with regular vascular structure. **c** Round hypoechoic B-NHL LN with echoes from the core biopsy needle (arrow); the hilum can no longer be recognised in the B-mode scan. **d** Central vascular supply with regular tree-like branching and slight peripheral vascularization.



▶ **Fig. 15** 56-year-old patient with mycosis fungoides (T-cell lymphoma). **a** B-mode scan of a superficial elongated LN (Solbiati Index > 2) with its structure maintained (cortex, medulla, hilum). **b** Colour Doppler clearly shows a hypervascularised LN with a regular vascular structure.

not uncommon [20]. From the oncological point of view, an expert examination of the LN histology is usually required to determine the subtype on which the treatment and prognosis depend.

Without any knowledge of the clinical background, it can be very difficult or even impossible to differentiate with certainty between lymphoma and inflammatory/reactive LNs on the basis of the ultrasound findings alone (▶ **Fig. 15**). Non-Hodgkin lymphomas are usually hypoechoic and strongly vascularised with a tree-like branching vascular structure. The cortex is typically thickened and hypoechoic, occasionally small typical hypoechoic nodules can be found in the cortex and medulla (▶ **Fig. 13a, 14a, 15a**). A complete cystic transformation may also be a typical ultrasound feature of NHL. Depending on the subtype, several affected LNs may show great ultrasonographic variation in a single patient.



▶ **Fig. 16** **a** Pelvic veins with unilateral venous dilatation of the leg veins, showing spontaneous echoes from the valves in the proximal femoral vein. **b** Loss of the spontaneous echoes after venous compression. **c** Venous compression leading to stenosis of the external iliac vein by pathological LNs. **d** Accelerated flow seen in the area of stenosis (colour Doppler). **e** Morphological presentation of the stenosis in B-Flow procedure.

As non-Hodgkin lymphoma in particular can compress the blood vessels, lymphoma must also be considered when there is unilateral dilatation of the leg veins with signs of venous stasis (▶ **Fig. 16a–c**).

Conflict of Interest

The authors declare that they have no conflict of interest.

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