

Lymphovascular invasion (Core)

Lymphovascular invasion (LVI) is an important prognostic indicator in endometrial carcinoma and documenting the presence or absence of this is a core element. LVI can be confidently diagnosed at the invasive front of a carcinoma when there is a tumour embolus within an endothelial-lined channel.¹⁻⁴ The embolus frequently takes the shape of the vessel lumen and may be attached to the endothelium. The tumour embolus usually resembles the endometrial carcinoma, but LVI associated with microcystic, elongated and fragmented (MELF) invasion may contain single or clustered histiocytoid or metaplastic-appearing cells that resemble the myometrial invasive cells of MELF.^{1,5}

There are several types of artefact that simulate LVI: these include artefacts secondary to tumour disruption; MELF pattern myometrial invasion; and retraction artefacts.^{1,2,6,7} The first situation is predominantly encountered in the setting of laparoscopic and/or robotic surgery followed by dissection of the uterus before adequate fixation.⁶⁻¹⁰ Clues to the presence of this type of artefact include fragments of tumour and, sometimes, normal constituents around the cut surfaces of the section, in tissue 'cracks', in large, medium-sized and small vessels, both adjacent to the tumour's invasive front and in distant locations.^{1,2} Often the amount of tumour within vessel appears disproportionate, for example in a tumour which is low grade and low stage. It may be impossible to distinguish 'real' LVI amongst all the artefact; this should be expressed in the surgical pathology report. Adequate fixation before prosection, generally lessens the degree of artefact. The second artefact type results from the morphologic similarity between MELF myometrial invasion and LVI.¹¹ Adding to the complexity is that MELF myometrial invasion is, indeed, associated with LVI.¹² The distinction between the two can usually be resolved by knowing about this type of artefact and careful examination to differentiate between endothelium on one hand (LVI) and tumour cells floating in a microcyst lined by flattened and attenuated epithelium (MELF myometrial invasion). Immunohistochemical endothelial markers can sometimes be used to confirm a suspicion of LVI, especially when there is extensive retraction artefact. Epithelial markers, in addition, may be added to the panel when MELF myometrial invasion is present, although the literature is not consistent on the added value of immunohistochemistry (IHC) after haematoxylin and eosin (H&E) evaluation.^{4,13}

The absence of LVI is defined as no tumour cells within vessels.¹⁴ There is controversial data regarding the cut off for 'extensive' or 'substantial' LVI. 'Extensive' is defined as the presence of three or more vessels containing tumour, according to International Society of Gynecological Pathologists recommendations,¹⁴ but five or more vessels in the 2020 World Health Organization Classification¹⁵ and in the European Society of Gynaecological Oncology (ESGO)-European Society for Radiotherapy and Oncology (ESTRO)-European Society of Pathology (ESP) guidelines.¹⁶

Recent data indicate that 'substantial' or 'extensive' LVI is associated with adverse outcomes when compared to carcinomas with 'focal' or 'no' LVI.¹⁷⁻¹⁹ Although there have been different proposals for what constitutes extensive LVI, it is a good rule of thumb to diagnose extensive LVI when it is easily recognisable at scanning magnification (and artefact is excluded) and when present in three or more vessels on closer inspection. Recording the degree of LVI (focal or substantial/extensive) is regarded as a non-core element. LVI should not be included in the assessment of depth of myometrial invasion, or indeed, in determining any element of pathologic staging.⁴ LVI features in many (but not all) multivariate clinical outcomes analyses and is associated with lymph node metastasis, local and distant recurrence and poor survival.^{17,18,20} Thus, the presence of substantial LVI may highlight the need for adjuvant treatment, such as recommended in the 2020 ESGO-ESTRO-ESP consensus guidelines.¹⁶ A value of 'indeterminate' should be used sparingly and only in cases where there is genuine doubt. In such cases, it may be useful to report the reason for a response of 'indeterminate'.

References

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