

Do you use elastin stains to look for extramural (large vessel) venous invasion in colorectal carcinoma?

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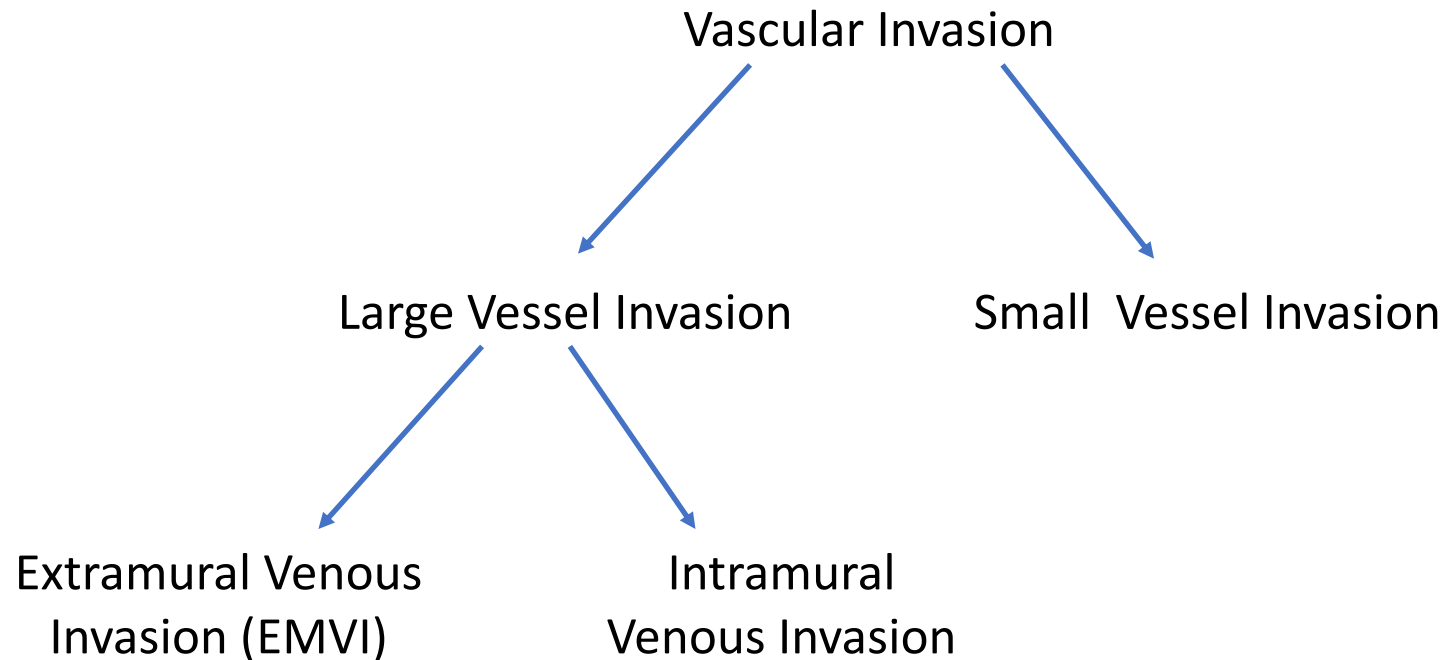
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Vascular Invasion is a Recognized Prognostic Factor

- Vascular invasion is a recognized negative prognostic factor in most cancers, including CRC
 - Included as standard part of most cancer templates as a required reporting element



Extramural venous invasion can be difficult to detect

- EMVI can be difficult to distinguish from small vessel LVI on H&E
- Situations where EMVI can be missed on H&E
 - Radiation related changes
 - EMVI present within advancing edge of tumor
 - Tumor obliteration of venous wall
- Poor inter-observer reliability in diagnosing EMVI
 - Littleford et al: GI pathologists had poor to moderate agreement (kappa 0.29 – 0.59) in reporting EMVI
 - Kirsch et al: Both GI and non-GI pathologists had poor agreement (kappa 0.22) in detecting EMVI as well as variation in reporting its presence

Variation in Reporting of EMVI in Patients with CRC

Royal College of Pathologists of UK and Australasia

Deepest level of venous invasion:
None ☐ / Intramural ☐ / Extramural ☐

Intramural vein invasion	Single selection value list: <ul style="list-style-type: none">• Not identified• Present
Extramural vein invasion	Single selection value list: <ul style="list-style-type: none">• Not identified• Present
Small vessel invasion	Single selection value list: <ul style="list-style-type: none">• Not identified• Present• Present and extensive

College of American Pathologists

Lymphovascular Invasion (select all that apply) (Note E)

☐ Not identified
☐ Present
 + ☐ Small vessel lymphovascular invasion
 + ☐ Large vessel (venous) invasion
 + ☐ Intramural
 + ☐ Extramural
☐ Cannot be determined

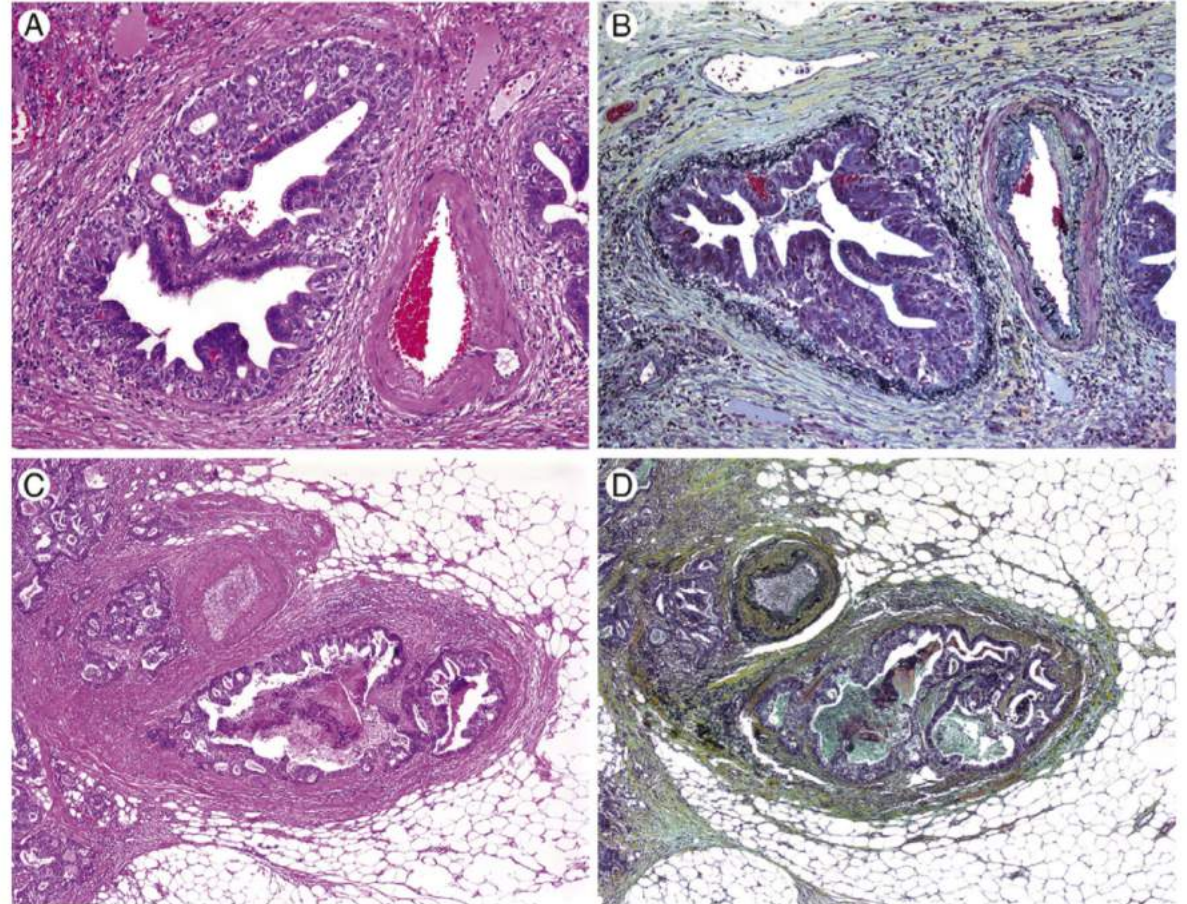
CAP protocol does NOT require separate reporting of small and large vessel invasion

Extramural venous invasion: Why is it important to report?

- Although simple to group together, EMVI and small vessel LVI have different prognostic implications
- EMVI is an independent indicator of poor prognosis
 - Associated with increased risk of recurrence and aggressiveness (e.g. development of visceral metastases)
 - In study of 268 Dukes' B CRC resection specimens, EMVI was independently associated with worse survival (HR 2.70, 95%CI 1.61- 4.53)
- Presence of EMVI can alter clinical management
 - Adjuvant chemotherapy can be offered if EMVI is detected in stage II colorectal carcinoma

Histologic features of EMVI (H & E+ Elastin)

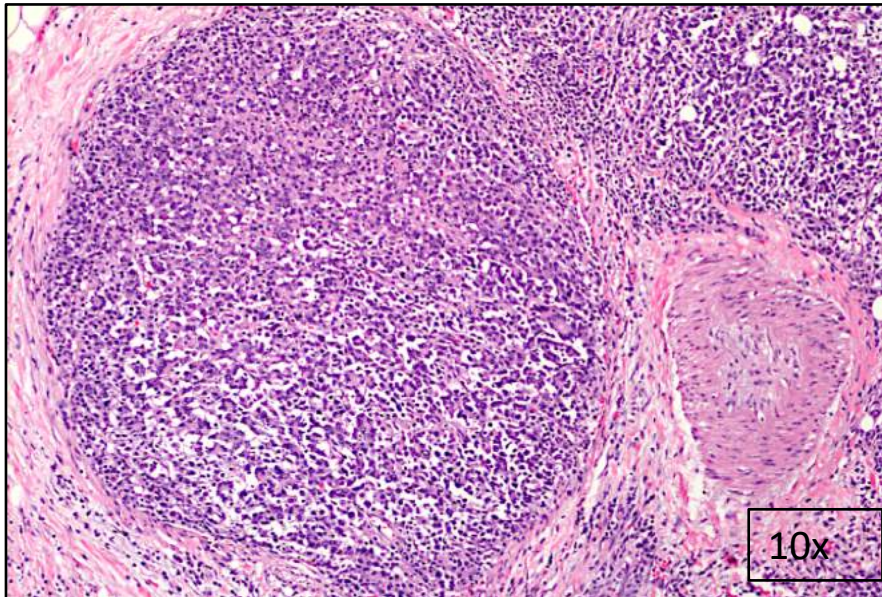
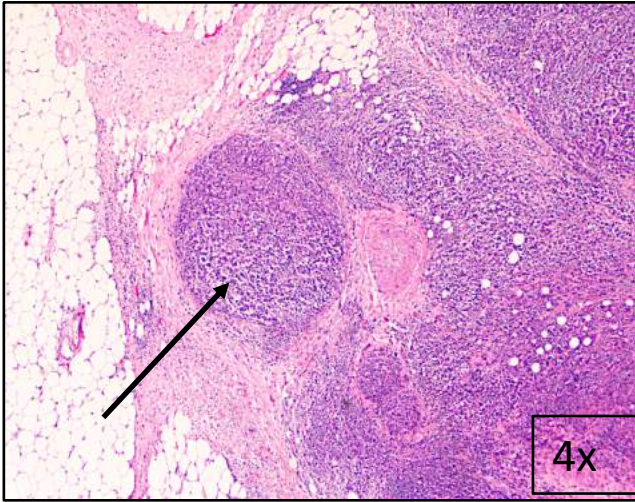
- “Orphan arteriole sign”
- “Protruding tongue sign”



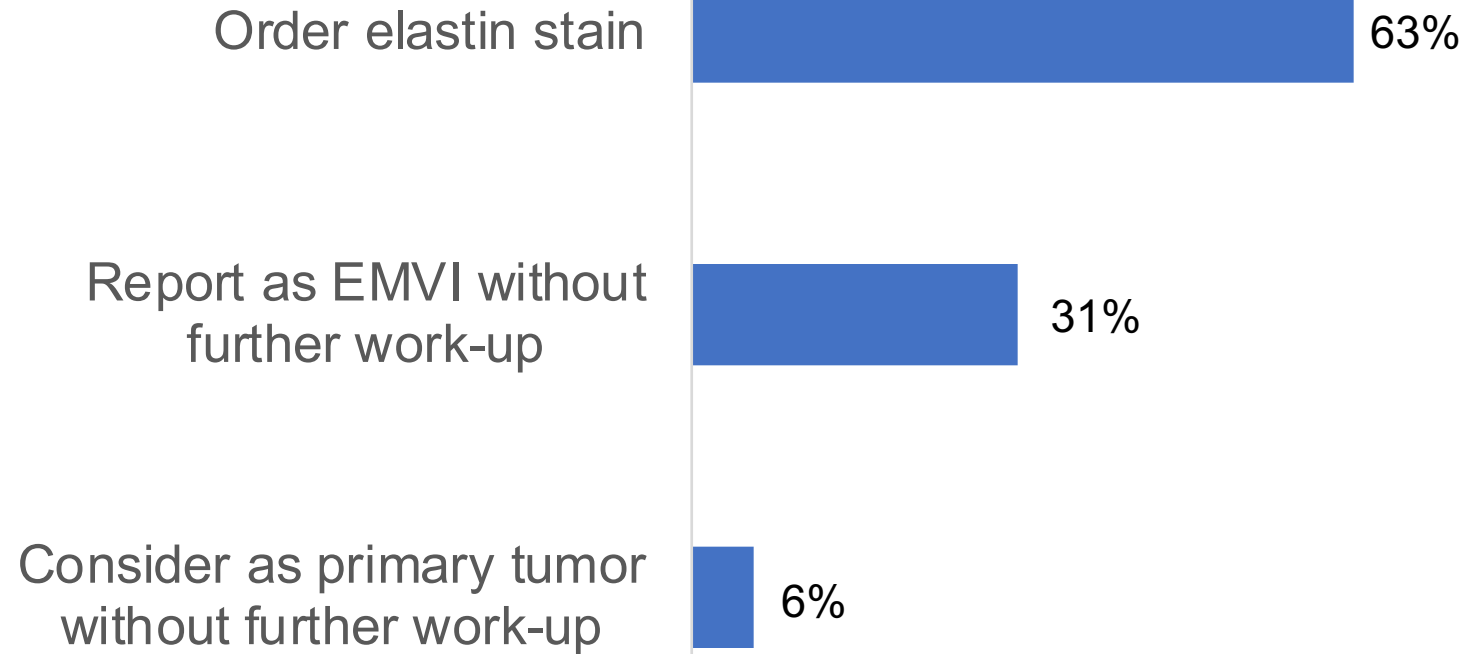
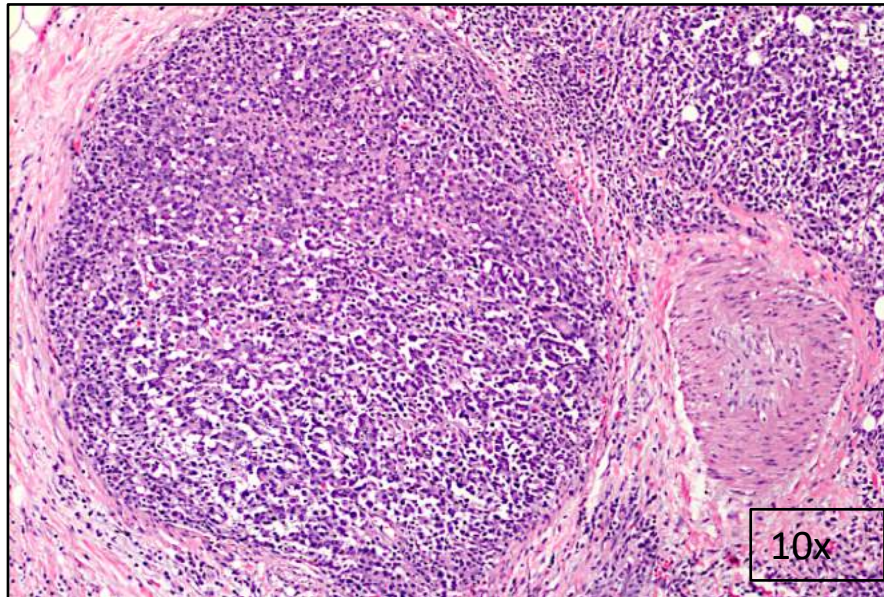
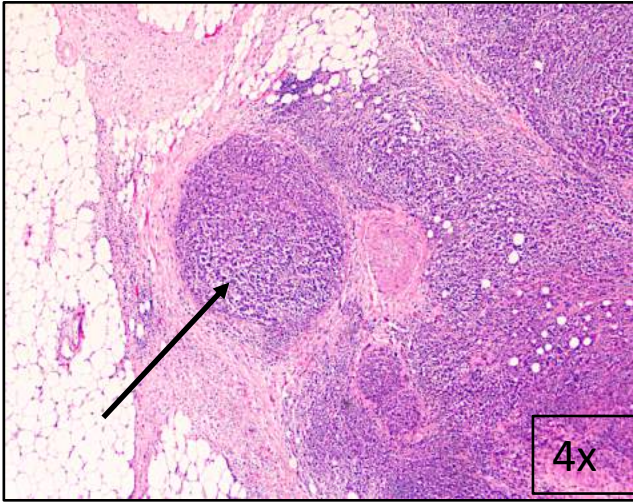
Do you use elastin stains to look for EMVI in colorectal carcinoma?



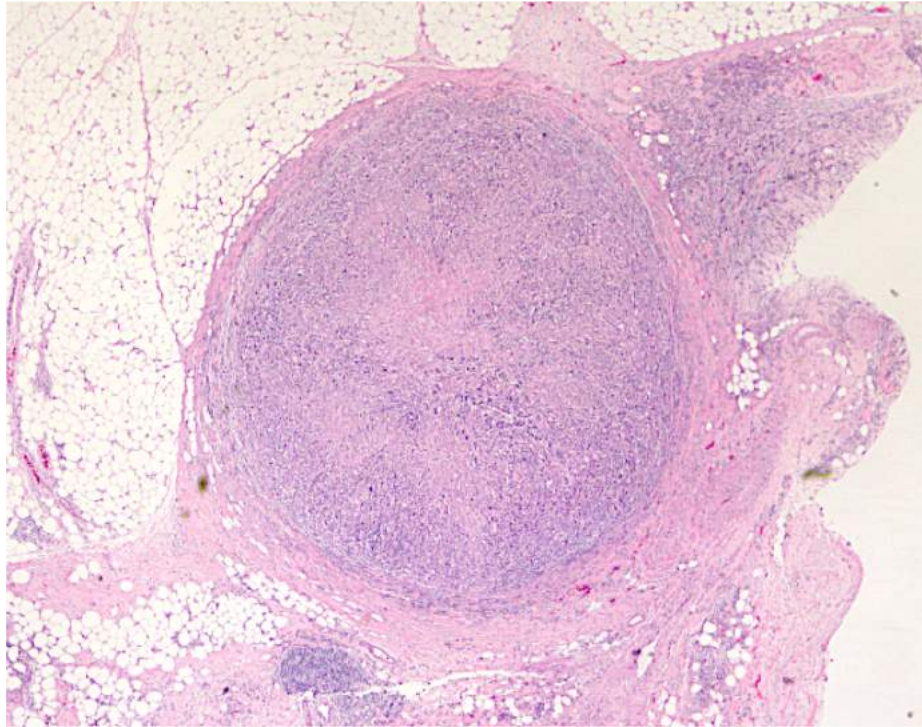
What would you do if you saw this nodule in a case of colonic adenoCA invading into pericolic adipose tissue?



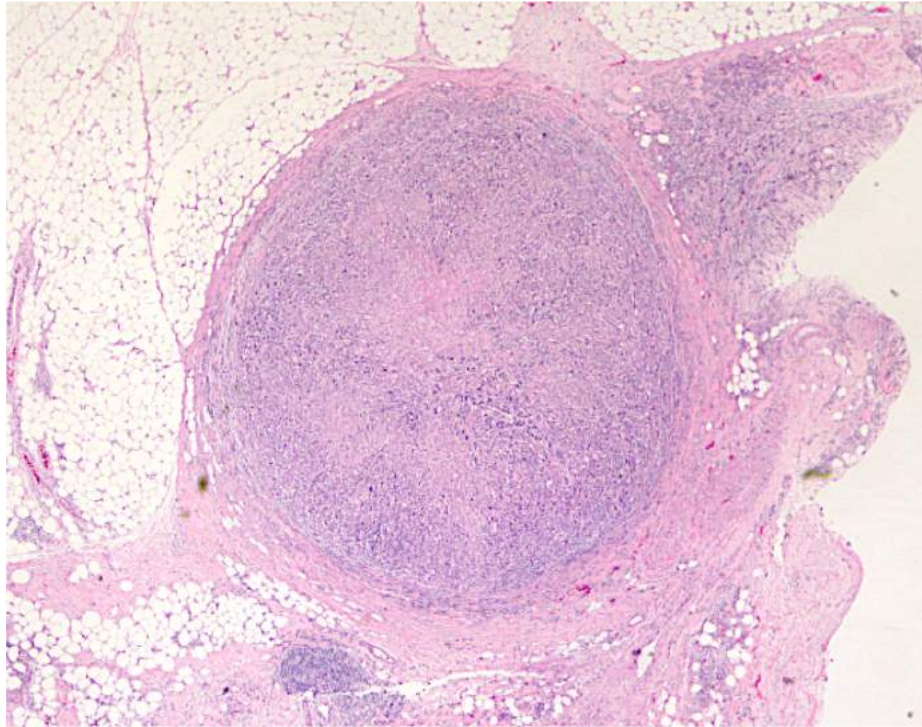
What would you do if you saw this nodule in a case of colonic adenoCA invading into pericolic adipose tissue?



How would you classify this nodule in a case of poorly differentiated colonic adenoCA from a 50 year old woman? A large artery and several lymph nodes were also seen.



How would you classify this nodule in a case of poorly differentiated colonic adenoCA from a 50 year old woman? A large artery and several lymph nodes were also seen.



Unsure, order elastin stain

59%

EMVI

19%

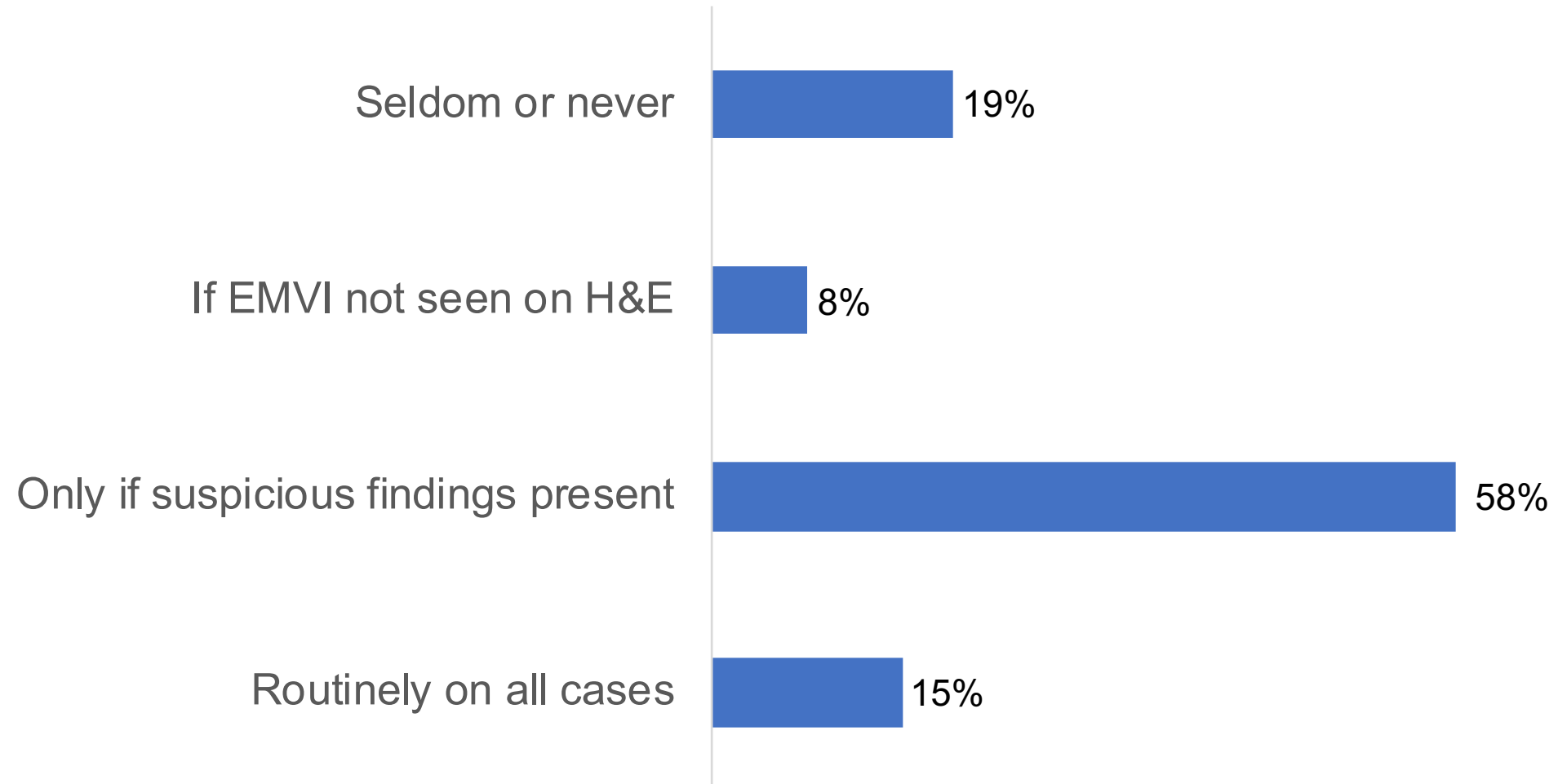
Tumor deposit

13%

Positive lymph node

9%

When do you order an elastin stain to look for EMVI in colorectal carcinoma?



Do Elastin Stains Help Detect EMVI Compared to H&E?

Author	H&E alone	Elastin Stain	P-value
Vass et al (n=75)	24%	43%	p<0.001
Abdulkader et al (n=498)	35%	46%	p=0.014
Kirsch et al (n=40)*	20%	46%	p<0.01
Kingston et al (n=50)	10%	48%	P=0.0001

- Also showed improved interobserver agreement from K=0.22 on H & E only to k=0.36 with elastin (GI and non-GI pathologists)

Does Use of an Elastin Stain Help Beyond Improving Detection of EMVI ?

- Use of elastin stain to highlight EMVI may provide prognostic information
 - Roxburgh et al demonstrated detection of EMVI using elastin was better than H & E alone in predicting 3-year cancer specific survival
 - VI detected by elastin stain only was associated with decreased survival on univariate and multivariate analyses
- Sejben et al showed that venous invasion highlighted by orcein stain were associated with synchronous or metachronous distant metastases ($p=0.01$); venous invasion detected by H & E only was not associated ($p=0.31$)

Recommendations

- Royal College of Pathologists (UK): at least 30% of CRC resections should have VI
- Multiple studies advocate for routine elastin staining on CRC tumor blocks because of significantly improved detection

Study	Recommendation
Dawson et al	<ul style="list-style-type: none">-Minimum 4-5 tumor blocks should be submitted-Elastin stain on any H&E equivocal for VI-If 30% benchmark not met, elastin should be done on all tumor blocks
Messenger et al	<ul style="list-style-type: none">-Minimum 4-5 tumor blocks should be submitted-Elastin stain on any H&E equivocal for VI-Consider performing elastin on all full-thickness tumor blocks, or at least those equivocal for VI
Abdulkader et al	<ul style="list-style-type: none">-Routine staining of all tumor blocks with elastin-Minimal increase in cost; improved turn around time

Conclusion and Future Directions

- EMVI has prognostic importance in patients with colorectal carcinoma
- Elastin stains significantly improve the detection of EMVI in colorectal carcinoma
- Some authors advocate that elastin stains should routinely be done on multiple tumor blocks vs. only if histologic features are suspicious for EMVI
- Standardized guidelines regarding the routine use of elastin stains, and incorporation of those guidelines in colorectal carcinoma reporting templates may be helpful to improve overall detection and reporting of EMVI on a broader scale