Multifactorial scoring systems (Non-core)

Several multifactorial scoring systems have been developed for assessment of malignant potential in adrenal cortical neoplasms. Some of the more commonly used ones are presented below along with their intended uses. There is ongoing debate around the validation and reproducibility of these systems so the International Collaboration on Cancer Reporting (ICCR) is unable to recommend any particular approach. ICCR has therefore chosen to ensure that pathologists record as consistently as possible the individual data items that contribute to the scoring systems (core data). Pathologists should use their judgement to select the appropriate system for their practice and individual tumour types.

1. Weiss system[1] for conventional adrenal cortical neoplasms

- High-nuclear grade (yes/no)
- Mitotic count of >5 mitoses per 50 HPFs (yes/no)
- Presence of atypical mitotic figures (yes/no)
- <25% lipid-rich (clear) cells (yes/no)
- Presence of diffuse architecture (yes/no)
- Presence of tumour necrosis (yes/no)
- Presence of venous invasion (yes/no)
- Presence of lymphatic (sinusoidal) invasion (yes/no)
- Presence of capsular invasion (yes/no)

The Weiss system can be deployed for the majority of conventional adrenal cortical tumours, but should not be used for oncocytic tumours because they consistently display densely eosinophilic cytoplasm, a diffuse architecture and high nuclear grade. The Weiss system consists of 9 elements, each worth one point. Tumours with Weiss scores ≥3 are considered to possess malignant potential and should be diagnosed as carcinomas.

2. Modified Weiss system (Aubert)[2] for conventional adrenal cortical neoplasms

- 2 x Mitotic count of >5 mitoses per 50 HPFs (yes/no)
- 2 x <25% lipid-rich (clear) cells (yes/no)
- Presence of atypical mitotic figures (yes/no)
- Presence of tumour necrosis (yes/no)
- Presence of capsular invasion (yes/no)

The modified Weiss system can be also deployed for the majority of conventional adrenal cortical tumours, but should not be used for oncocytic tumours. The modified Weiss system places twice the weight on mitotic rate and percent lipid-rich cells and eliminates nuclear grade, architecture, venous invasion and lymphatic invasion. Tumours are thereby graded from 0 to 7, with those tumours scoring ≥3 possessing malignant potential. The modified Weiss system is highly correlated with the original Weiss system.[2]

3. Lin-Weiss-Bisceglia system[3] for oncocytic adrenal cortical neoplasms

Major criteria

- Mitotic count of >5 mitoses per 50 HPFs (yes/no)
- Presence of atypical mitotic figures (yes/no)
- Presence of venous invasion (yes/no)

Minor criteria

- Tumour size >10 cm and/or weight <200 g (yes/no)
- Presence of tumour necrosis (yes/no)
- Presence of lymphatic (sinusoidal) invasion (yes/no)
- Presence of capsular invasion (yes/no)

The Lin-Weiss-Bisceglia system is used specifically for oncocytic adrenal cortical neoplasm. Under the Lin-Weiss-Bisceglia system, pathologic features are divided into Major and Minor criteria. The presence of any Major criterion indicates malignant potential. In the absence of Major criteria, the presence of 1-4 Minor criteria indicates uncertain malignant potential.

4. Helsinki system[4] for diagnosis and prognosis of conventional and oncocytic adrenal cortical neoplasms

- 3 x Mitotic count of >5 mitoses per 50 HPFs (yes/no)
- 5 x Presence of tumour necrosis (yes/no)
- + Ki-67 proliferation index (percentage)

Tumours with Helsinki scores >8.5 predict metastatic behaviour. The Helsinki score was evaluated and validated using conventional and oncocytic tumours.[5]

5. Reticulin algorithm[6,7] for the diagnosis of conventional and oncocytic adrenal cortical neoplasms

- Abnormal/absent Reticulin framework (yes/no)
- Presence of tumour necrosis (yes/no)
- Mitotic rate of >5 mitoses per 50 HPFs (yes/no)
- Presence of venous invasion (yes/no)

The Reticulin algorithm employs a two-step process. First, the reticulin framework is evaluated by silver-based histochemical staining for reticulin (see **Note 20 RETICULIN FRAMEWORK**). If disruption of the framework is observed, then the tumour is evaluated for the presence of the criteria above. Tumours with both disrupted reticulin framework and at least one of the other diagnostic criteria are considered to possess malignant potential and can be diagnosed as carcinoma.

6. Algorithm for paediatric adrenal cortical neoplasms

- Tumour weight >400 g (yes/no)
- Tumour size >10.5 cm (yes/no)
- Extra-adrenal extension (yes/no)
- Invasion into vena cava (yes/no)
- Presence of venous invasion (yes/no)
- Presence of capsular invasion (yes/no)
- Presence of tumour necrosis (yes/no)
- Mitotic count of >15 mitoses per 20 HPFs (yes/no)
- Presence of atypical mitotic figures (yes/no)

The above Wieneke/Armed Forces Institute of Pathology (AFIP) algorithm[8] reflects the observation that paediatric adrenal cortical neoplasms generally behave better than their adult counterparts despite similar histologic features, which also may reflect their different genomic landscapes.[9] Additional efforts to include the Ki-67 proliferation index into the evaluation of paediatric tumours are ongoing.[9,10] For these reasons, evaluation of paediatric tumours with Ki-67 is recommended whenever possible.

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