N-cadherin, also known as Cadherin-2 (CDH2) or neural cadherin (NCAD) is a protein that in humans is encoded by the CDH2 gene.

Clinically non-functioning pituitary neuroendocrine tumors (NF-PitNETs) present a varying degree of aggressiveness, and reliable prognostic markers are lacking. Øystese et al. aimed to characterise the distribution of E-cadherin and N-cadherin in corticotroph, PIT1 and null-cell NF-PitNETs, and link it to the course of the tumours.

The distribution of E-cadherin and N-cadherin was investigated by immunohistochemistry in a retrospective cohort of 30 tumours of the less common NF-PitNETs (corticotroph (N = 18), PIT1 (N = 8) and null-cell PitNETs (N = 4)). Immunoreactive scores (IRS) were compared to previously presented cohorts of gonadotroph NF-PitNETs (N = 105) and corticotroph functioning PitNETs (N = 17).

They found a low IRS for the extracellular domain of E-cadherin (median 0 (IQR 0-0, N = 135)), a medium to high IRS for the intracellular domain of E-cadherin (median 6 (IQR 4-9)) and a high IRS for N-cadherin (median 12 (IQR 10.5-12)) throughout the cohort of NF-PitNETs. The corticotroph NF-PitNETs presented a higher IRS for both the extra- and intracellular domain of E-cadherin (median 0 (IQR 0-1) and median 9 (IQR 6-12), respectively) than the gonadotroph NF-PitNETs (p < 0.001 for both comparisons). The presence of nuclear E-cadherin was associated with weaker staining for the intracellular domain of E-cadherin (median 4 (IQR 0.5-6) and median 9 (IQR 9-12), for tumours with and without nuclear E-cadherin, respectively), and with a lower rate of re-intervention (p = 0.03).

Considering the results and the benign course of NF-PitNETs, they suggest that a high N-cadherin and downregulation of membranous E-cadherin are not associated with a more aggressive tumour behaviour in these subgroups of NF-PitNETs<sup>1</sup>.

## 1)

Øystese KAB, Casar-Borota O, Berg-Johnsen J, Berg JP, Bollerslev J. Distribution of E- and N-cadherin in subgroups of non-functioning pituitary neuroendocrine tumours. Endocrine. 2022 Jun 8. doi: 10.1007/s12020-022-03051-6. Epub ahead of print. PMID: 35674926.

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