MATTERS ARISING

Letter to the editor regarding "Is Knosp enough? A novel classification for Acromegaly: a retrospective analysis of cure rates and outcome predictors in a large tertiary centre"

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Dear Prof. Mathiesen, Dear Tiit.

We read with great interest the recent article by Dr. Fayez and colleagues [3] on predictors of biochemical remission in patients with acromegaly. The article employs a substantial cohort with good surgical results. Within their analysis, Dr. Fayez and colleagues report on various radiological measurements that are potential predictors for outcome. They include an interesting analysis of measures such as intercarotid distances and tumor diameters, which we welcome – and the importance of which in defining the surgical corridor and endoscopic/microsurgical accessibility falls in line with the previous literature on the topic [7, 8, 12].

The novel measure that Dr. Fayez and colleagues describe is the "MI" ratio, which according to the instructions in their article is formed through:

1. On the coronal slice with the largest tumor diameter, measuring the *widest* intercarotid distance among the cavernous segments (I)
2. Measuring the distance from the most lateral border of the tumor to the midline. (M)
3. Dividing the two values (M/I)

The authors powerfully demonstrate that this measure is associated with biochemical remission, and also focus their argumentation on the fact that this is a continuous

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measurement (or indeed a measurement at all) compared to established discrete classifications such as modified Knosp [5], Hardy [4], and TRANSSPHER [6].

We applaud our colleagues on their work, and would like to draw their attention to a conceptually very similar scoring system previously described and externally validated by several groups, namely the Zurich Pituitary Score or ZPS (Fig. 1) [9, 10]. The measure has shown excellent generalizability and interrater reliability, and is calculated by:

1. Measuring the largest horizontal tumor diameter on a coronal slice
2. Measuring the *smallest* intercarotid distance among the intracvernous horizontal C4 segments
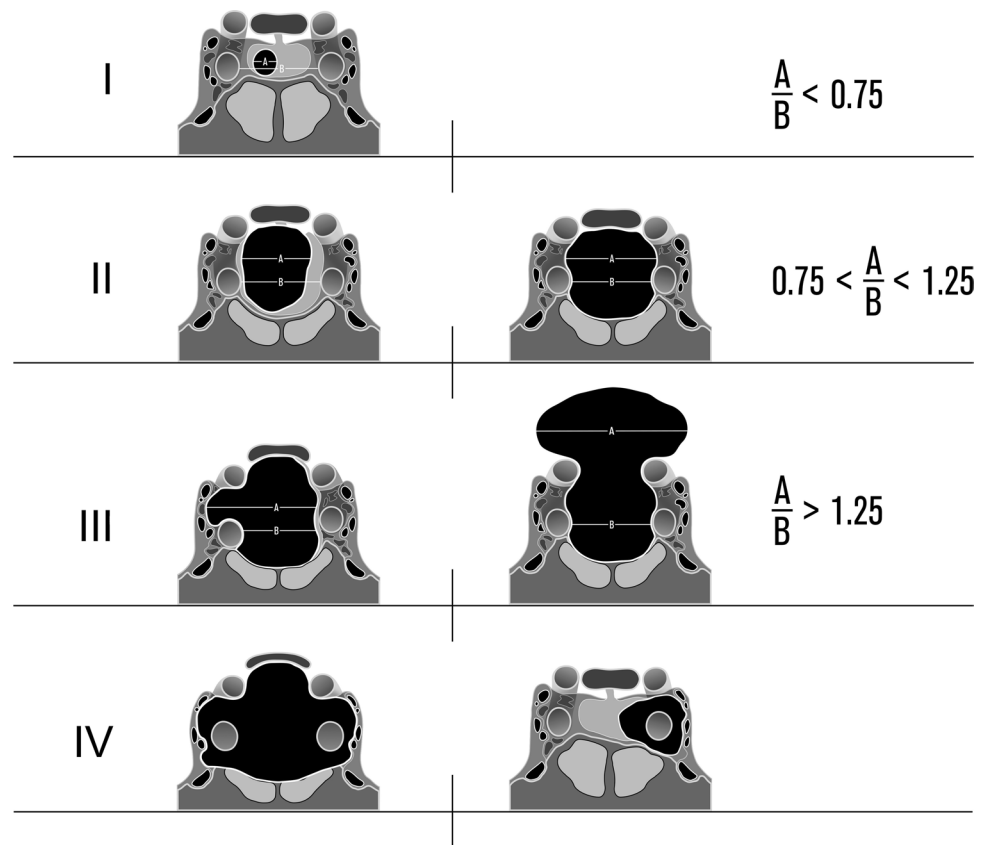3. Dividing the two values (ZPS Ratio), Checking complete 360° carotid encasement, and classifying accordingly

Both measures can and have been applied (as continuous ratios) to machine learning-based clinical prediction modelling [11]. There are two main differences among the MI and the ZPS: First, the ZPS is bilateral and not unilateral. Second, the ZPS uses the minimal intercarotid distance, instead of the widest intercarotid distance as described by the MI. While it might be said that unilaterality may be more suitable for laterally located microadenomas, we would argue that – as is the case with minimum vs. maximum intercarotid distance – these scores work by modelling the "bottleneck" of the surgical approach, which is determined by the smallest window between the C4 horizontal cavernous segments of the carotid [1, 2]. The relationship among the greatest horizontal tumor diameter and this intercarotid window – along with presence of any tumor directly lateral to the carotid – then determines resection potential (regardless whether uni- or bilaterally, and whether nonfunctioning or functioning).

Fig. 1 Ilustration of the Zurich Pituitary Score. The largest horizontal tumor diameter in the coronal plane (A) is divided by the minimal intercarotid distance at the level of the intracavernous horizontal C4 segment of the carotid (B). In addition, the presence of complete encasement of the carotid is checked to determine presence of ZPS IV

$$\frac{A}{B} < 0.75$$

$$0.75 < \frac{A}{B} < 1.25$$

$$\frac{A}{B} > 1.25$$

We congratulate Dr. Fayez and colleagues and value our colleagues' further investigation and validation of the concept of quantifying the surgical corridor.

Declarations

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