Epidemiology of Hypothalamic Obesity in Craniopharyngioma and Other Rare Sellar and Suprasellar Tumors

Witte J[1], Surmann B[1], Weinert M[1], Flume M[2], Touchot N[3], Beckhaus J[4], Friedrich C[4], Müller HL[4]

[1]Vandage GmbH, Germany; [2] Gene Access GmbH, Germany; [4] Rhythm Pharmaceuticals, USA; 4 Department of Pediatrics and Pediatric Hematology / Oncology, University Children's Hospital, Carl von Ossietzky University Oldenburg, Klinikum Oldenburg AöR, Germany

Introduction

Hypothalamic obesity (HO) is defined as abnormal weight gain resulting in severe persistent obesity due to physical, tumor- and/or treatment related damage of the hypothalamus. The epidemiology of HO is poorly understood. We developed a database algorithm supporting the standardized identification of tumor/treatment-related HO (TTR-HO) patients.

Methods

The algorithm was used to estimate incidence rates of TTR-HO patients in the German healthcare context from a representative claims database (n=5.42 million) covering 2010-2020. Patients were identified based on surgery/radiotherapy procedures and HO-associated tumor diagnoses (n=3,976). HO was defined by incident obesity and validated based on incident diabetes insipidus diagnosis and desmopressin prescription within a twelve-month period after surgery/radiotherapy. Uncertainty due to algorithm definitions was explored in sensitivity analyses.

Results

Estimated annual incidence of TTR-HO in Germany was between 0.7 and 1.7 cases per 1,000,000 persons (2019 prevalence: n=1,262 patients). A bimodal distribution of incident cases with HP in all age groups was identified: children/young adults aged 10-14 years and adults aged 40-44 years. Most frequent HO-validated tumor diagnoses were benign sellar/suprasellar tumors (6.1/1,000,000 persons over nine-years), including tumors of the craniopharyngeal duct (3.1/1,000,000), neoplasms of the pituitary gland (4.1/1,000,000), and nonspecific brain tumors of endocrine glands (2.4/1,000,000).

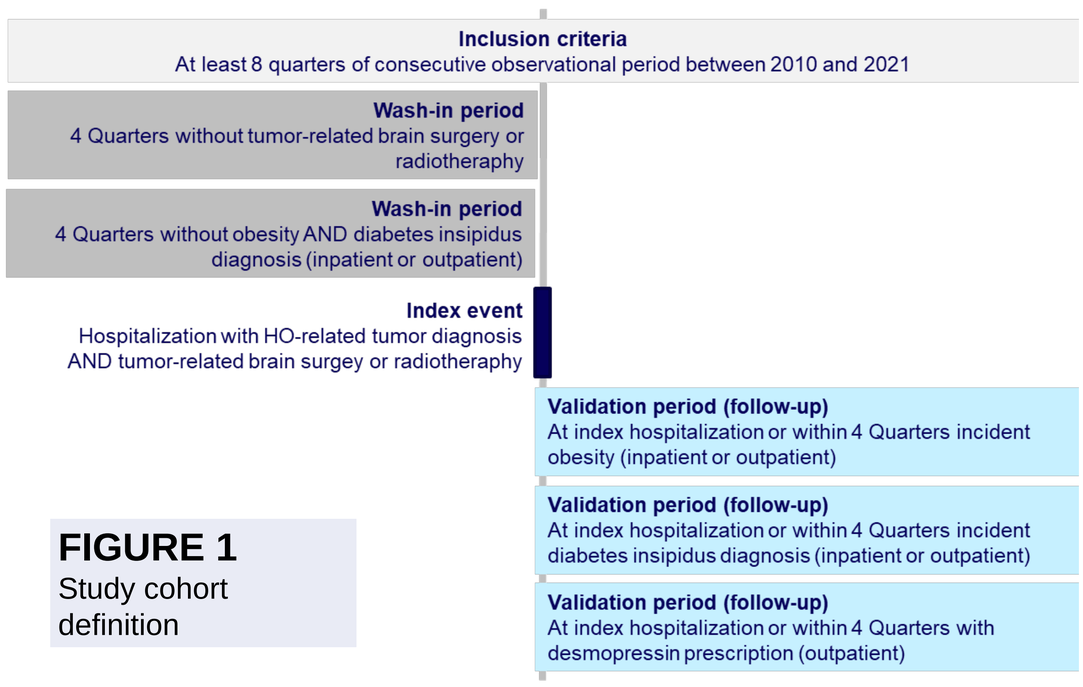

FIGURE 1 Study cohort definition

Table 1: Study population, validated HO population, estimated HO incidence rate and HO patient characteristics

	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Study population (N), (Million)	3.93	4.02	4.06	4.11	4.18	4.27	4.34	4.37	4.41	5.42
Patients with index hospitalization (n)	422	431	448	415	415	479	436	464	466	3,976
HO cases (n)	5	5	3	7	3	3	3	3	5	37
HO incidence rate (/100,000)	0.13	0.12	0.07	0.17	0.07	0.07	0.07	0.07	0.11	0.68
Mean age (SD)	40.0 (11.4)	44.0 (18.5)	44.3 (10.5)	38.4 (25.5)	26.3 (15.3)	47.3 (20.2)	31.7 (25.7)	22.7 (20.2)	40.0 (10.4)	38.0 (18.0)
Female (%)	40	60	33	86	100	33	33	67	60	59.5

Disclosures:
This study was funded by Rhythm Pharmaceuticals. Rhythm reviewed and provided feedback to the authors, but the authors had full editorial control and provided their final approval of all content. NT is an employee of Rhythm Pharmaceuticals. JW, BS and MW are employees of Vandage, which was paid by Rhythm Pharmaceuticals to conduct this research. JW owns shares of Vandage. MF received grants from Vandage. BJ, BS, HLM received no project specific grants.

Data availability:
Project-specific access to an anonymized, selected study data set for the analyses was provided by the GWQ ServicePlus AG. The data analyzed in this study are not publicly available due to data protection regulations and national legislation. All data-related processes of Vandage are under the data protection supervision of an external data protection officer.

Table 2: Nine-year HO-incidence per tumor entity and patient demographics

Tumor diagnosis (ICD-10-GM code)	HO incidence rate (/100,000)	Percentage of total cases (%)*	Mean age (SD)	Age groups, years (%)			Female (%)
				<20	20-64	65+	
Total	0.68	100	38.0 (18.0)	16.2	70.3	13.5	59.5
Benign neoplasm							
Brain, supratentorial (D33.0)	0.04	5.4	51.0 (12.7)	0	50	50	100
Brain, unspecified (D33.2)	0.02	2.7	25.0 (NA)	0	100	0	0
Cranial nerves (D33.3)	0.04	5.4	17.0 (9.9)	50	50	0	0
Pituitary gland (D35.2)	0.41	59.5	40.0 (16.2)	5	86	9	68
Craniopharyngeal duct (D35.3)	0.13	18.9	32.9 (22.7)	43	43	14	43
Neoplasm of uncertain or unknown behavior of endocrine glands							
Brain, unspecified (D43.2)	0.24	35.1	39.7 (20.9)	15	62	23	31
Pituitary gland (D44.3)	0.20	29.7	42.2 (15.3)	0	91	9	91
Craniopharyngeal duct (D44.4)	0.18	27.0	33.4 (20.7)	40	50	10	50
Unspecified (D48.9)	0.02	2.7	44.0 (NA)	0	100	0	0
Other histiocytosis syndromes (D76.3)	0.02	2.7	46.0 (NA)	0	100	0	0

* Diagnosis of two or more tumor entities per patient possible. "NA" Sample sizes are too small.

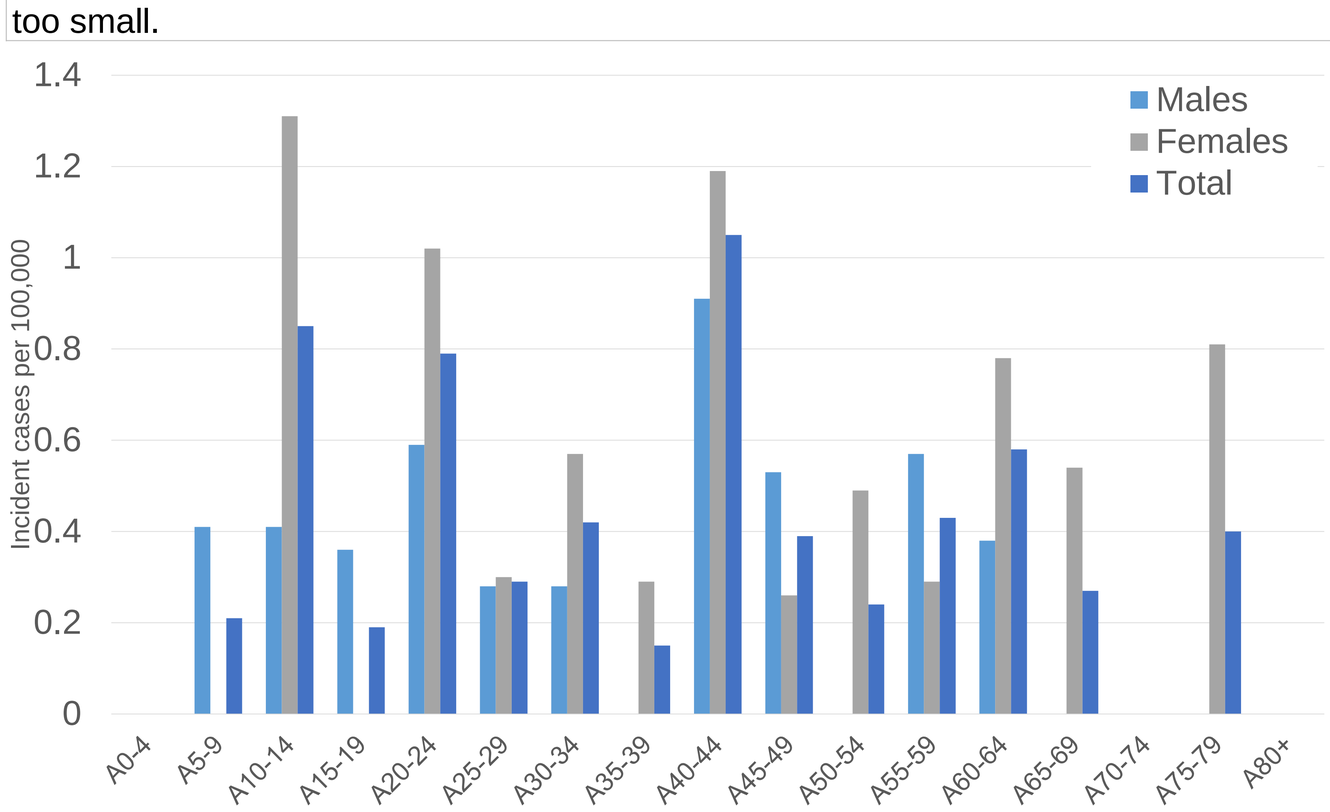

FIGURE 2 Estimated HO incidence rate per age and sex based on a rolling nine-year cohort

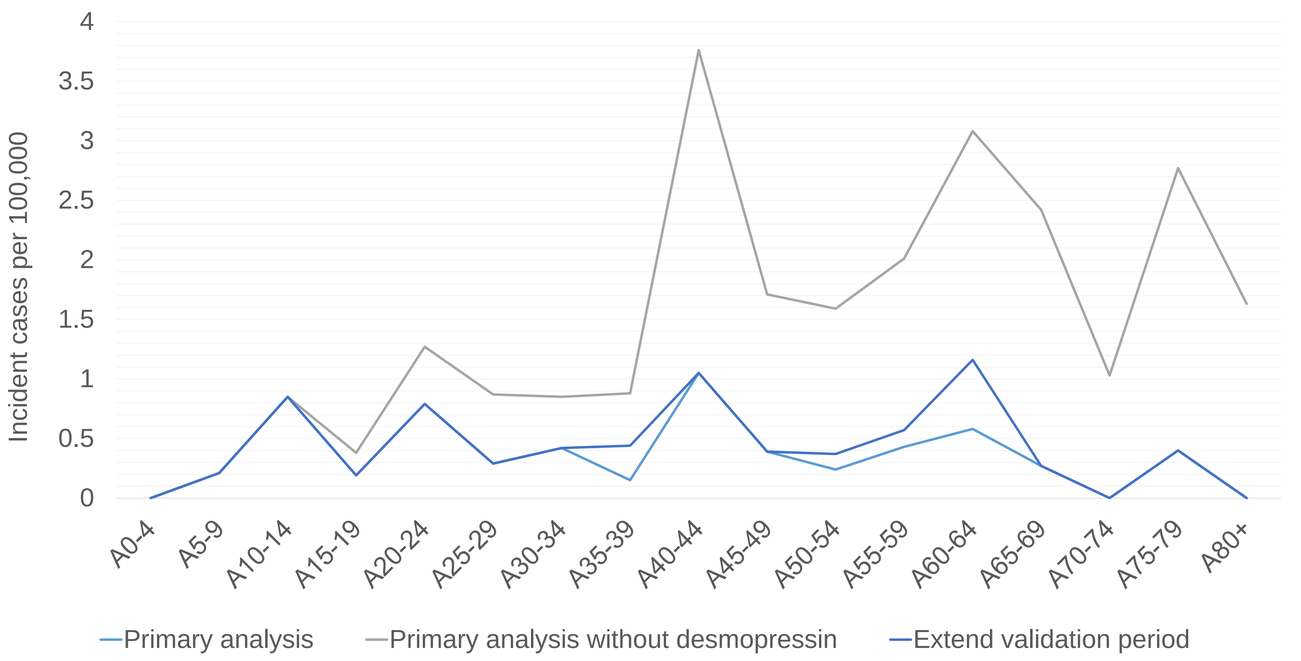

FIGURE 3 Sensitivity analysis on HO incidence rate per age group.

Conclusions

This is the first real-world database analysis of TTR-HO epidemiology, refining current estimates of HO-epidemiology and early patient identification. A more comprehensive characterization of HO patients, along with a better understanding of its clinical implications, will be crucial in developing optimal treatment strategies to improve patient outcomes.