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Epidemiology of meningiomas. A nationwide study of surgically treated tumours on French medico-administrative data

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ABSTRACT

Background: To describe the epidemiology of surgically treated meningiomas and compare the results with previously published studies.

Methods: We processed the French medico-administrative national hospital discharge summary database, Programme de Médicalisation des Systèmes d'Information (PMSI) using an algorithm combining the type of surgical procedure and codes from the International Classification of Diseases to retrieve appropriate cases of meningiomas operated between 2008 and 2016.

Results: This nationwide study found 25,737 cases of operated meningiomas. Global incidence of operated meningiomas equals 4.51, 95%CI[4.46–4.57] for 100 000 person-years and increased over the last 9 years. Benign neoplasms account for 91.3%, neoplasms of uncertain or unknown behaviour for 6.2% and malignant for 2.5%. There is a decrement of female over male ratios as the malignancy potential progresses. Incidence of operated meningiomas was 3 times more frequent in women than men. Mean age at surgery was 57.6 years for women and 59.5 for men. The incidence of meningioma surgery increases with age and is maximal for the 60–64 years category. Only 0.4% of operated patients were under 18 years.

Meningioma surgeries of the cranial convexity and the middle skull base are the most common.

Conclusion: The PMSI database is a reliable and effective source for studying the epidemiology of surgically treated meningiomas, including the precise location of the tumour. Our findings comfort previous studies and are comparatively correlated. This may assert the usefulness of such a database to investigate the patients' outcome after meningioma surgery.

1. Introduction

Meningiomas which are thought to arise from arachnoidal cap cells are the most common intracranial extracerebral tumours. The 2016 World Health Organization (WHO) classification of tumours affecting the central nervous system (CNS) recognises three grades of meningioma [1]. WHO grade I meningiomas occur for two-thirds in women and are associated with a relatively good outcome. Grade III which are rare, have an aggressive growth pattern and a poor outcome [2]. Behaviour and outcome of atypical - WHO grade II meningiomas, are intermediate [3]. Decision to treat a meningioma is based mainly on one criterion: is the tumour symptomatic? Complete surgical excision is the treatment of choice for all meningiomas. Surgical approach is based on skull flap cutting to expose the dural insertion of the tumour given its origin outside of the brain parenchyma. Principles include: a tailored keyhole craniotomy to minimise exposure of other structures and brain injury; if necessary, a careful and progressive displacement of anatomical structures to reach the meningioma; coagulation and/or section of the infiltrated dura mater; debulking of the meningioma respecting the arachnoid plane; preservation of the surrounding arteries, veins and nerves for skull base meningiomas; meticulous but gentle haemostasis; reconstruction and closure of the dura mater ideally with pediculated epicranium; anatomical osteosynthesis of bone flat; skin closure as usual; goal: total removal (Simpson grade I/II) at first surgery or maximal safe resection [4,5].

Further optimal management is difficult to establish, the role of post-operative radiotherapy as a standard adjuvant treatment remains controversial apart for grade III [3,6,7]. Only a handful studies have

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Table 1
Distribution of operated meningioma by year and grade, with related incidences.

Global French population[a]		Years									Total
		2008 62 134 866	2009 62 465 709	2010 62 765 235	2011 63 070 344	2012 63 375 971	2013 63 697 865	2014 64 027 958	2015 64 300 821	2016 64 558 472	
Benign neoplasm of meninges (D32)	n =	2 485	2 438	2 447	2 503	2 709	2 594	2 722	2 760	2 847	23 505
(WHO grade I)	Incidence[b]	4.00	3.90	3.90	3.97	4.27	4.07	4.25	4.29	4.41	4.12
Neoplasm of uncertain or unknown	n =	171	196	209	180	129	153	200	171	191	1600
behaviour of meninges (D42)	Incidence[b]	0.28	0.31	0.33	0.29	0.20	0.24	0.31	0.27	0.30	0.28
(WHO grade II)											
Malignant neoplasm of meninges (C70)	n =	67	72	57	67	54	71	68	80	96	632
(WHO grade III)	Incidence[b]	0.11	0.12	0.09	0.11	0.09	0.11	0.11	0.12	0.15	0.11
Total		2 723	2 706	2 713	2 750	2 892	2 818	2 990	3 011	3 134	25 737
Global incidence[b]		4.38	4.33	4.32	4.36	4.56	4.42	4.67	4.68	4.85	4.51
95%CI[c]		4.22-4.55	4.15-4.50	4.16-4.49	4.20-4.53	4.40-4.73	4.26-4.59	4.50-4.84	4.52-4.85	4.69-5.03	4.46-4.57

[a] At the 1st January of the considered year (https://www.insee.fr/fr/statistiques/3312958).
[b] For 100 000 person-years.
[c] Calculated by Poisson generalized linear model (https://cran.r-project.org/web/packages/epitools/index.html).

investigated the nationwide incidence of meningioma in Europe or elsewhere in the world [8–11]. Epidemiology of tumours is mainly provided by cancer registries, often limited to a designated geographic area and/or not including benign neoplasms, despite international recommendations. In recent years, healthcare databases have been increasingly used for epidemiological purposes. To date, such a research on meningiomas has not been achieved in France. The objectives of this study were to assess the epidemiology of operated meningiomas in France using the National Healthcare database and to compare our findings with published results.

2. Material and methods

We performed a nationwide descriptive observational retrospective study. The data were extracted from the French medico-administrative national hospital discharge summary (PMSI for Programme de Médicalisation des Systèmes d'Information) database, gathering discharge abstracts from all hospitals in France, public and private. The patients who underwent the surgical resection of a meningeal tumour between 2008 and 2016 were included. Direct identification of meningioma surgical cases is not possible. Therefore, we used an algorithm combining two variables [12,13]. Firstly, one associated to an intracranial extracerebral tumour surgery identified by the "Common Classification of Medical Acts" (CCAM) which aims to describe more precisely medical and surgical procedures on a common basis, both for hospital and ambulatory care (http://www.atih.sante.fr/ccam-descriptive-usage-pmsi-2017). The CCAM is fully comprehensive as it contains details of each of the 7200 procedures and services, corresponding to only one label and one code. Thus, there is no ambiguity, and it is quite easy to use. Meningiomas may grow everywhere along the cerebrospinal axis, including from inside the ventricle. However, they generally spread from some typical locations. The CCAM enables us to know the precise site of the tumour origin. Some locations *e.g.* petroclival are infrequent, making them unsuitable for statistical analysis. Therefore, a simplified and practical classification was designed, following description usually used in the literature. Forty CCAM codes were categorised into 8 anatomical locations (Supplementary material 1). A second variable related to the primary diagnosis of a meningeal neoplasm according to the International Classification of Diseases (ICD-10) was taken into account to refine our search. Throughout the PMSI and over the years, a patient is identified by the very same number, regardless the institution to which he or she was admitted. Therefore, a patient was counted only once even if he or she had multiple neurosurgical procedures in different centres. WHO grade I meningiomas were considered as corresponding to the D32, grade II as D42 and grade III as C70. Incidental tumours never operated are not documented in the PMSI. Therefore, only surgically treated meningioma were taken into account for this studies. The crude incidence rate of operated meningioma was calculated over the whole study period, for the total study population and, separately, for men and women. National, regional and age-adjusted incidence rates were calculated by the direct method using the French population's figures provided by the National Institute of Statistics and Economic Studies (https://www.insee.fr/en/accueil). To enable international comparisons, standardised incidence rates based on a direct standardization model were also calculated with USA (2000 U.S.A. Standard), worldwide (World (WHO 2000–2025) Standard) and Europe (2010 European Standard) populations as references (https://seer.cancer.gov/stdpopulations/, https://ec.europa.eu/eurostat/data/database). Ninety five per cent confidence intervals were calculated using Poisson generalized linear model. Descriptive statistics, analysis and graphics were performed with both the SAS Enterprise and the R programming language and software environment (R version 3.5.1 (2018-07-02)) for statistical computing and graphics, the epitools and ggplot2 package among other [14–16] The statistical programme and workflow was written in R Markdown v2 with RStudio® for dynamic and reproducible research [17]. *P*-values < 0.05 were considered as statistical significance. This study was conducted according to the ethical guidelines for epidemiological research in accordance with the ethical standards of the Helsinki Declaration (2008) and the French data protection authority (CNIL), an independent national ethical committee, authorisation number: 2008538 [18]. The RECORD guidelines for studies conducted using routinely-collected health data were followed [19].

3. Results

3.1. Institutions, surgical activity

A total number of 25,737 meningiomas were surgically treated over a 9-year period (Table 1). One hundred and twenty centres were involved with a median annual activity of 0.9 procedures, IQR (interquartile range)[0.2, 35.3]. 51.7% of the centres had one or less procedure per year. 37.5% of the centres performed ten or more procedures per year. 3558 tumours *i.e.* 13.8% of all meningiomas were removed at our institution "Assistance Publique-Hôpitaux de Paris (AP-HP)" which comprises 6 different neurosurgical departments. Save for institutions which have a small meningioma surgery activity of less than 9 procedures per year (our institution (AP-HP) excluded too), the median activity is of 38.8 procedures per year IQR[18.9, 65.1]. 77.5% of the meningiomas were operated in 31 university hospitals, 10% in 63

Table 2
Operated meningiomas' age-adjusted incidences by standard population and category of age.

Age Category	Incidence rates adjusted on the standard population of			
	France	USA[a]	World[b]	Europe[c]
0-1	0.04	0.05	0.07	0.04
1-4	0.06	0.07	0.09	0.05
5-9	0.05	0.06	0.07	0.04
10-14	0.11	0.14	0.16	0.1
15-19	0.21	0.25	0.29	0.21
20-24	0.36	0.39	0.49	0.39
25-29	0.85	0.9	1.11	0.99
30-34	1.77	2.02	2.17	2.05
35-39	3.01	3.69	3.27	3.31
40-44	4.86	5.75	4.62	5.12
45-49	7.01	7.35	6.15	7.35
50-54	8.46	7.94	6.79	8.74
55-59	8.68	6.49	6.1	8.58
60-64	10.16	6.48	6.21	9.68
65-69	11.61	8.36	7.22	11.37
70-74	11.45	9.64	6.7	12.23
75-79	9.09	7.04	3.96	8.59
80-84	6.21	3.9	1.99	5.12
85+	2.27	1.3	0.53	1.49
0-100	**4.51**	**3.88**	**3.26**	**4.53**
95%CI	[4.46-4.57]	[3.83-3.93]	[3.22-3.3]	[4.48-4.59]

[a] USA (2000 U.S.A. Standard) – https://seer.cancer.gov/stdpopulations/.
[b] World (WHO 2000–2025) Standard – https://seer.cancer.gov/stdpopulations/.
[c] 2010 European Standard – https://ec.europa.eu/eurostat/data/database.

private institutions, 6.4% in 10 "semi-private" institutions and, 6.1% in 16 general hospitals. In university hospitals, the mean annual activity was 71.5 procedures *vs.* 4.6 for private institutions, 18.2 "semi-private" institutions and 10.8 for general hospitals. This difference is highly significant ($p < 0.001$). Median duration of hospital stay was 9 days, IQR [7,13].

3.2. Incidences of operated meningiomas

Global crude incidence rate of operated meningiomas equals 4.51, 95%CI[4.46–4.57] for 100 000 person-years (Table 1). USA, worldwide and Europe age-standardised rates respectively are: 3.88, 95%CI [3.83–3.93], 3.26, 95%CI[3.22–3.3] and 4.53, 95%CI[4.48–4.59] for 100 000 person-years (Table 2 & Fig. 6). Benign neoplasms of the meninges account for 91.3%, neoplasms of uncertain or unknown behaviour for 6.2% and malignant for 2.5%. Incidences look somewhat stable over the 9-year period, save for the benign tumours which show a slight increase of frequency (Table 1 & Fig. 1). For the year 2012, there is a noticeable peak in benign neoplasm incidence. Nonetheless, there is a significant increase of meningioma surgeries, all grades combined (4.38 in 2008 *vs.* 4.85 in 2016; p-value = 0.0014), mainly due to the growth of benign meningioma's resections count (4 in 2008 *vs.* 4.41 in 2016; $p = 0.0025$) but, not of neoplasm of uncertain or unknown behaviour of meninges ($p = 0.667$) or malignant ones ($p = 0.118$) (Fig. 1B).

3.3. Distribution by gender

As expected, meningioma surgery was 3 times more common in women than men (74.98% *vs.* 25.02%) (Table 3 & Fig. 2). The difference of percentages between female and male diminishes as the malignant potential increases, but, malignant neoplasms of the meninges are still more frequent in female with 58.86% (Fig. 2). Ratios of female over male are 3.13 for benign lesions, 2.24 for uncertain behaviour and 1.43 for malignant tumours. The decrement of female over male ratios as the grade progresses is significant (χ^2 $p < 0.001$) (Fig. 2).

3.4. Distribution by age

For the whole population, mean age at surgery was 58.1(SD 13.8) years; 57.6 (SD 13.4) years for the women and 59.5 (SD 15) for the men (Table 3). This 2-year difference is significant ($p < 0.001$). There is also a significant difference of age at surgery between female and male for benign (2 y., $p < 0.001$) and malignant tumours (4.3 y., $p = 0.0036$) but not for those of uncertain behaviour (1.3 y., $p = 0.128$). The incidence of meningioma surgery increases with the age and, is maximal for the 50–55 year category for the female gender *vs.* for 60–65 year category for the male (Fig. 3). Only 0.43% is under 18 years.

3.5. Distribution by location

Meningiomas of the cranial convexity are the most common (24.4%) followed by middle skull base (21.6%) (sphenoïd wing) (Fig. 4). Spinal tumours account for 9.8%. A calculation with the ICD-10 last digit D32.**1**, D42.**1**, & C70.**1** = spinal meninges, returns 9.4%, a slight but nonetheless significant difference (McNemar's test $p < 0.001$).

The malignant ratio defined as: number of uncertain + malignant cases over benign tumours, is maximal for the "Parasagittal" location and minimal for the "Anterior skull base" location, intraventricular excluded. We could not find a pattern of malignant ratio distribution but there is a decreasing trend for skull base-located tumours. We further summarise these categories, excluding intraventricular tumours, into 2 new ones. Cranial convexity, parasagittal and falx cerebri locations are merged into a new broader" convexity" class and, anterior, middle, posterior skull base and spine into the" skull base" class. A 2×2 contingency table comparison of benign *vs.* uncertain + malignant by "convexity" (convexity, parasagittal & falx) *vs.* "skull base" (anterior, middle & posterior fossa and spine) shows a small but significant more frequent occurrence of aggressive meningiomas on the "convexity": 9.48% *vs.* 8.03% (χ^2 $p < 0.001$).

3.6. Geographical incidence

Departmental incidences of meningioma are heterogeneously distributed across the country. Patients operated on for a benign neoplasm of the meninges are mainly from South of France departments (n° 04, 05, 13, 83) in the Provence-Alpes-Côte d'Azur region (PACA). Malignant meningiomas mostly occur also in South of France, in Occitanie and Nouvelle Aquitaine departments (Fig. 5; based on patient's postal address at surgery). Departments with the lowest incidences of surgically treated benign (2.09), uncertain (0) and, malignant (0) meningiomas are the n° 62, n° 04 and, n° 16 respectively. *I.e.* in 6 departments no patient with a malignant meningioma was diagnosed as well as 7 departments with no case of meningioma of uncertain or unknown behaviour. Departments with the highest incidences of surgically treated benign (5.88), uncertain (1.02) and, malignant (0.51) meningiomas are the n° 83, n° 10 and, n° 09 respectively (Fig. 5).

4. Discussion

Meningiomas are very common tumours of the central nervous system, unlike data on their epidemiology as well as their risk factors. Management varies significantly according to factors such as clinical presentation, age, tumour location, size, and associated pathology. Treatment options include observation with radiological follow-up, radiation therapy, surgery or combinations of these alternatives. Extent of resection is the most powerful factor which correlates to the survival and the relapse but, treatment paradigms vary among surgeons, institutions and countries. Most meningiomas exhibit an indolent behaviour and frequently silent course and, more than 80% are graded

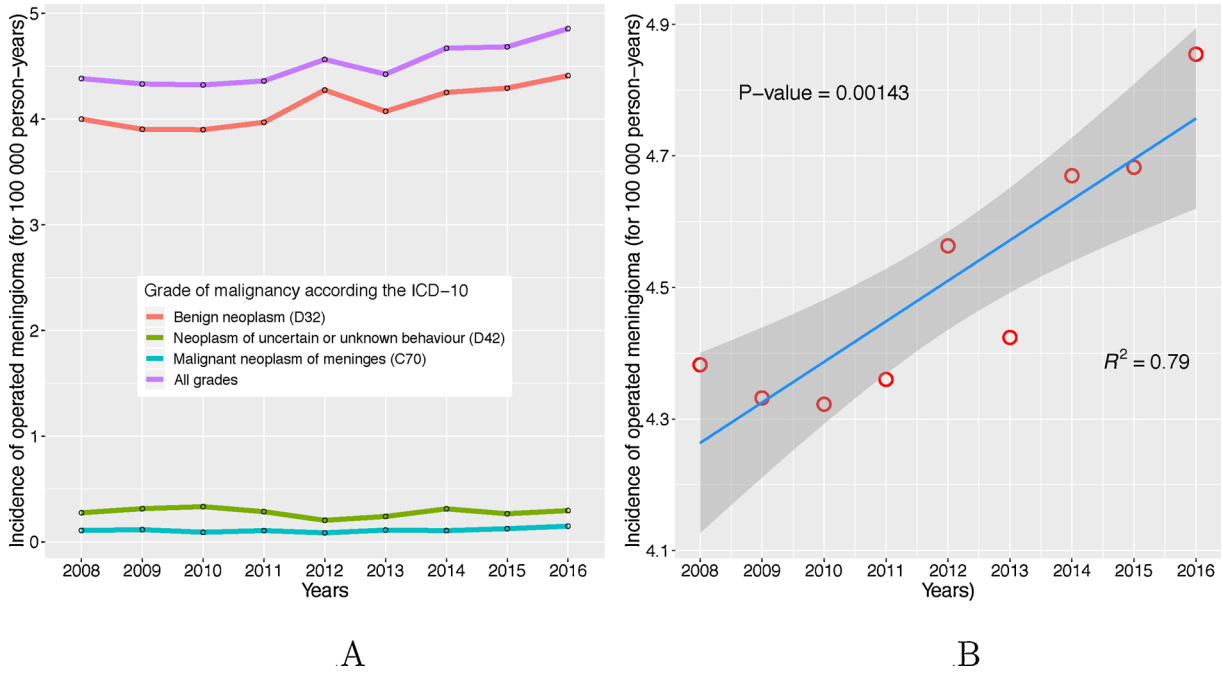

Fig. 1. A. Evolution of operated meningioma incidences by grade over the 9-year period. B. Linear regression of operated meningioma incidences over the 9-year period.

Table 3
Distribution of operated meningiomas by the gender and grade with related mean age at surgery, between 2008 and 2016.

Grade	Statistics	Gender		Total
		Female	Male	
Benign neoplasm of the meninges	Count (n =)	17,820	5685	23,505
(IDC-10: D32)	Proportion[a]	69.2%	22.1%	91.3%
(WHO grade I)	Mean age at surgery	57.6 (SD 13.3) y.	59.5 (SD 14.9) y.	< **0.001**[b,c]
Neoplasm of uncertain or unknown behaviour of the meninges	Count (n =)	1106	494	1600
(IDC-10: D42)	Proportion[a]	4.3%	1.9%	6.2%
(WHO grade II)	Mean age at surgery	57.4 (SD 13.6) y.	58.8 (SD 15.3) y.	0.13[b,c]
Malignant neoplasm of the meninges	Count (n =)	372	260	632
(IDC-10: C70)	Proportion[a]	1.4%	1%	2.5%
(WHO grade III)	Mean age at surgery	57.2 (SD 13.5) y.	61.5 (SD 16.4) y.	< **0.001**[b,c]
All grades combined	Count (n =)	19298	6439	25,737
(IDC-10: D32 + D42 + C70)	Proportion[a]	75%	25%	100%
(WHO grade I, II & III)	Mean age at surgery	57.6 (SD 13.4) y.	59.5 (SD 15) y.	< **0.001**[b,c]

[a] Percentages of the 25,737 operated meningiomas.
[b] Student's t-test.
[c] *P*-values displayed in **bold** reached the statistical significance.

benign (I) according to the last WHO classification [1]. However, the overall 5-year survival is less than 70% and declines with the patient's age [20]. Moreover, for completely removed benign meningiomas the 5-year rate of recurrence is about 20% [21]. Thus, the aggressive course of some meningiomas and the apparent incidence rise should promote further research considerations.

4.1. Strengths and limitations

The strengths of the PMSI database reside both in the high number of patients and in the exhaustive data available from every hospital in the country. Quality control is carried out a posteriori by medical inspectors on samples. However, the PMSI has some limitations in its use. Even if coding rules are national, there may be differences between establishments. The algorithm we used to identify surgically treated meningioma cannot be formally validated, and some patients may not have been identified. The PMSI database has been created for payment purposes. Its main limitation is the lack of case validation. The anonymisation makes it difficult to match clinical cohort with PMSI data to perform such a validation, as only events accompanying the diagnosis or complicating the disease are encoded [22]. Only removed meningiomas were taken into account in this study. Tumours solely treated by (stereotactic) radiotherapy were not included. Incidental tumours never operated or irradiated regarding their small size and/or absence of growth and those followed in outpatient clinics are not documented in the PMSI. Therefore, incidences found may be lower compared to

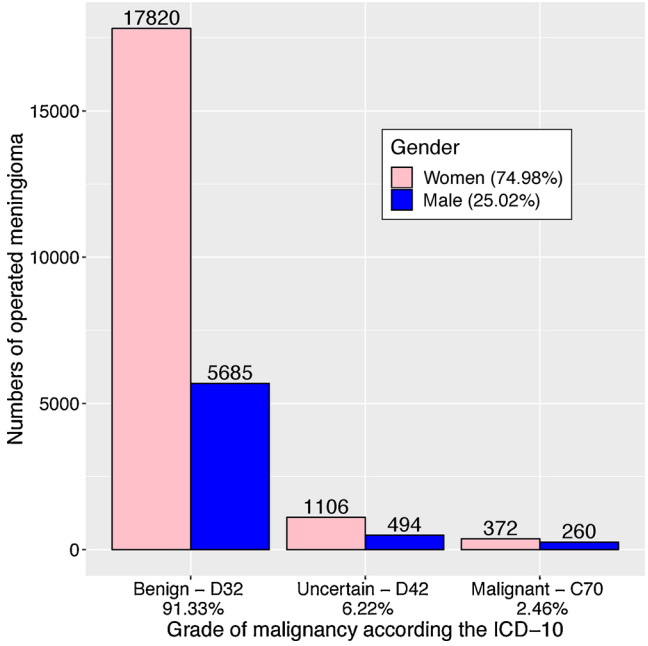

Fig. 2. Distribution of operated meningiomas by grade of malignancy and gender.

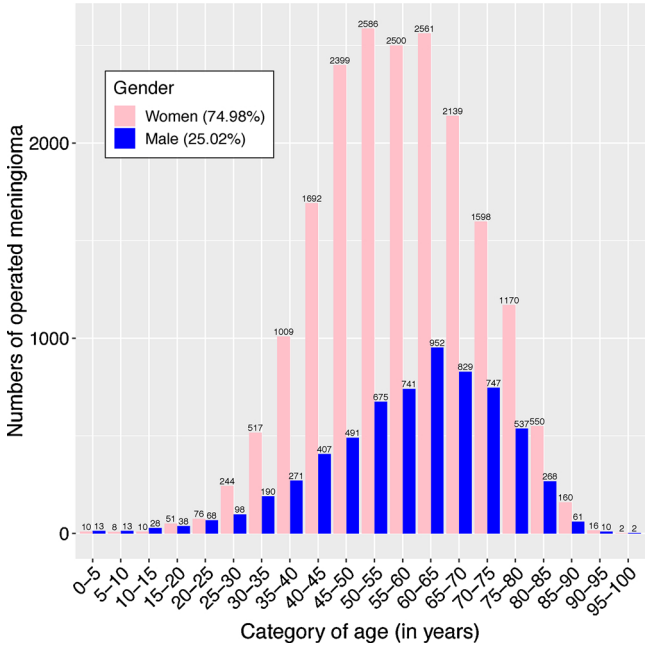

Fig. 3. Distribution of operated meningiomas by category of age and gender.

real ones, as we did not take into account meningioma under clinical and radiological surveillance. Regarding this bias, the PMSI database seems more appropriate for investigation of treated meningiomas and associated outcome rather than for real incidence estimation.

4.2. Incidence

Our result of 4.51 is within the range of reported French rates and close to those found by Zouaoui et al. of about 4.2 and by Elia-Pasquet et al. of 4.4 [8,23]. Reported incidences across the world vary from 1.58 to 8.71 [10,11,21,24–26]. The most recent CBTRUS report estimated meningioma incidence to be 8.14 per 100 000 in the United States for the 2010–2014 period [20]. Only 2 studies on meningioma

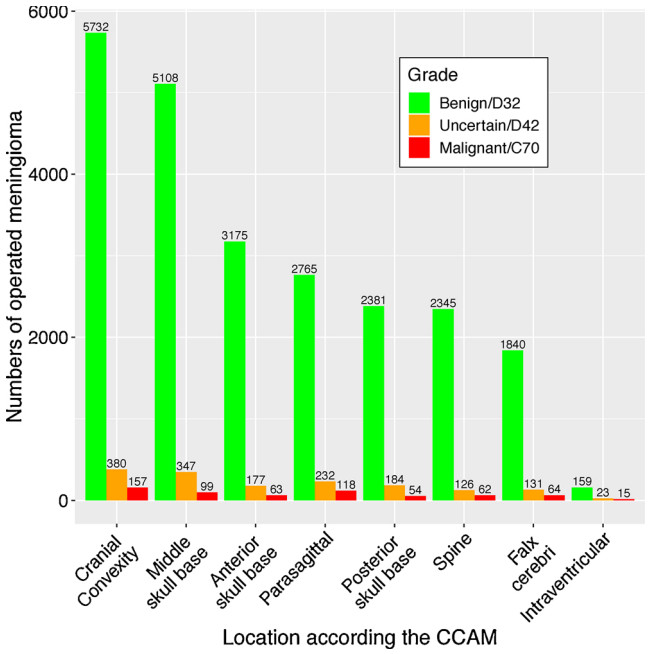

Fig. 4. Distribution of operated meningiomas by grade of malignancy and location according to the CCAM.

epidemiology have been conducted in France, one being limited to the department of Gironde [8,23,27]. The incidence reported by the Gironde registry, the first and only in France including benign and malignant CNS tumours and, also meningioma-like neoplasms without histological confirmation, is of 6.52 per 100 000 person-years for the 2000–2011 period [21]. On the contrary, the study by Zouaoui et al. is based on the French Brain Tumour database, counting only meningioma with histological validation and like in our study only removed neoplasms were considered. Our study is a nationwide surgical-based investigation, like most cancer registries who collected cases according to histology reports which can be solely provided by a surgical procedure [9,10]. Comparison between studies is difficult by variations in adjustment procedures. Age adjusting is a way to make fairer comparisons between groups with different age distributions. Comparison rates from different sources supposes the use of the same standard population as it is not legitimate to compare adjusted rates which use different standard populations. Some publications present crude incidence rates while others are standardised on national, USA or world population or do not provide the specific population of reference. We standardised our crude incidence rates on 3 specific standard populations *i.e.* 2000 U.S.A. (3.88), World 2000–2025 (3.26) and Europe 2010 (4.53). Despite some similarities, there are still significant differences as for example, some registries include cases without histological confirmation, 28.7% in CBTRUS data.

4.3. Variations of incidence

Our results show a significant rise of all and mainly benign meningiomas (p-value = 0.0014). In addition, a peak of incidence of benign meningioma is visible for the year 2012, associated with a small depression in uncertain behaviour the very same year. We did not find an explanation for this. Several studies suggested a frequency increase over the time [26]. However, Cea-Soriano et al. found that the incidence of meningioma in the United Kingdom remained stable over the 12-year study [11]. Despite contrasting findings, increasing incidences of meningioma may be confounded from increasing numbers of operated patients due to the modifications of the surgical practices. Although intracranial tumours are rare, incidences may gradually increase worldwide due to among others, the development of diagnostic

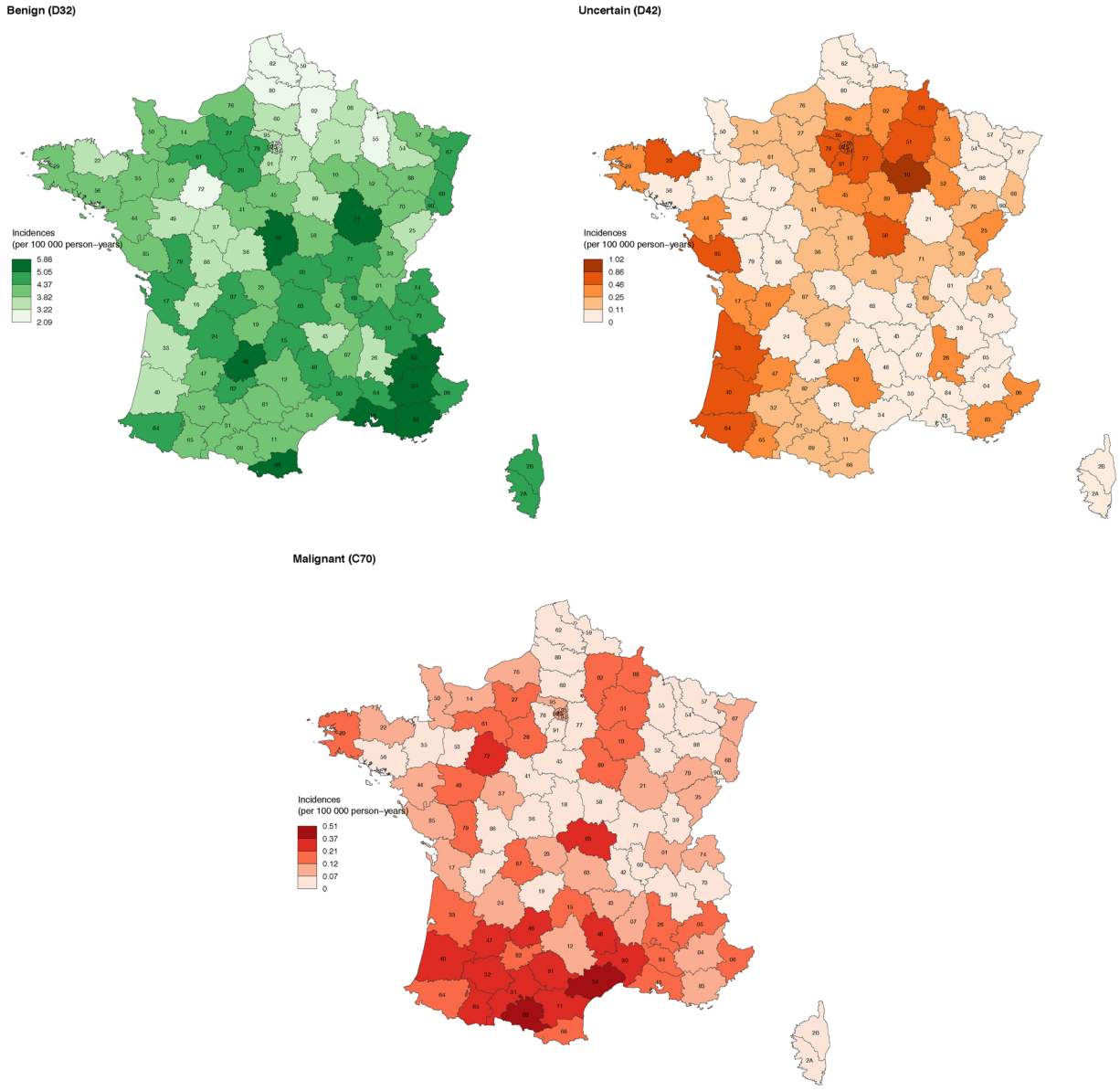

Fig. 5. Departmental incidence according to patient address, of benign, uncertain and malignant operated meningioma in France.2008–2016.

technologies, greater access to brain imaging and improved medical care. The incidences' increase we observed may have several yet, uncertain explanations. There may have been not only improvements in the ICD-10 and CCAM coding accuracy but, also changes in potential risk factors. Interestingly, our results were obtained over a nine-year period when no major medical care modification happened. Another source of potential bias may be the surgeon or multidisciplinary team (MDT) preference of operate *vs.* watchful wait or radiation treatment.

4.4. Gender

Across populations, incidence of brain tumours is consistently related to sex, with opposite patterns for meningiomas and gliomas. The female predominance of meningiomas was identified by Harvey Cushing a century ago. Women are three times as likely as men to be operated on for a meningioma [21]. No convincing hypothesis has been provided to explain this difference. A growing body of evidence suggests the influence of sexual hormones although most cases occur in menopausal women. Malignant meningiomas seem to be more frequent in male patients. Our results are fairly consistent with this finding as there is a significant decrement of the sex ratio along with the malignant potential growth, from 3.13 for benign lesions to 1.43 for malignant tumours (Fig. 2).

4.5. Age

As expected, meningioma frequency is higher in the elderly and maximum for the 60–64 years category. Our study is focused solely on removed meningioma contrary to Baldi et al. who found a peak rate between 75 and 89 years, but consider all tumours, operated or not. At an advanced age above 80 years, patients are less likely to undergo surgery or to get a tissue-based diagnosis. This may explain the difference between our results. Incidence discrepancy may be even more biased in greater ages in the PMSI database *vs.* exhaustive registries. However, our results are similar to Zouaoui et al. who found a mean age at surgery of 57.7 *vs.* 58.1 (SD 13.8) years in the present study. In addition, graphical representations of the operated patients by category of age and gender are rather alike [8]. We confirmed that meningiomas are extremely rare in the paediatric population, with less than 1 case for 200 before 18 years [28]. Meningioma incidence is lower in

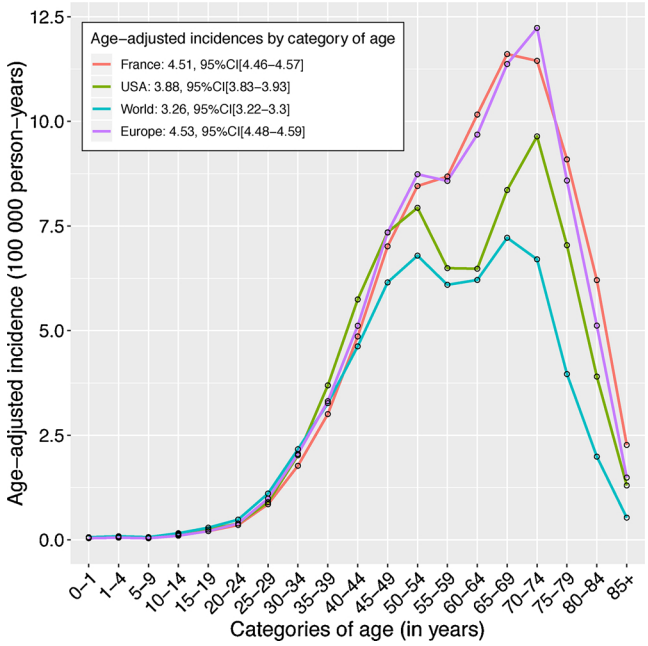

Fig. 6. Evolution of operated meningiomas' age-adjusted incidences by regions of the World and category of age.

(developing) countries where the population is younger [24]. Increasing life expectancy and use of medical imaging lead to a greater incidence of meningioma diagnoses, both symptomatic and asymptomatic. Therefore, it will be a growing common clinical concern as age above 80 years is an independent risk factor for any complication with a reported 1-year mortality rate of 9.4% [29,30].

4.6. Grading

Regarding the overall proportion of WHO grade I - D32 (91.33%), II - D421 (6.22%) and III - C70 (2.46%) meningiomas, our figures are close to those found by Kshettry et al. of 94.6%, 4.2%, 1.2% respectively [31]. We confirm that malignant meningiomas are rare, accounting only for 1–3% of all meningiomas with a stable incidence over the time around 0.11 *vs.* for 0.12 for the CBTRUS [2,20]. Although grade II meningiomas have traditionally been recognised in only about 5% of cases, after changes in diagnostic criteria with the 2007 and 2016 WHO CNS classifications, they nowadays comprise around 20% [1,32,33]. In the present study, the main error of grade classification affect the neoplasm of uncertain or unknown behaviour of meninges - D42 which we made to correspond with the WHO grade II. A substantial part of D42 tumours may be wrongly categorised as benign neoplasm of meninges because access to histology reports are not always granted to those who fill in the PMSI. The ICD-10 does not reflect the accuracy of the last WHO CNS grading system contrary to the ICD for Oncology (ICD-O-3.1; http://codes.iarc.fr/). The ICD-O is a domain-specific extension of the ICD for tumour diseases, which is widely used by cancer registries. The ICD oncology is based on the WHO classification of tumours affecting the central nervous system and there is a reverse grading correspondence between the two. For example, ICD-O-3.1 codes for WHO grade II are 9539/1 and 95538/1 and, 9530/3 and 9538/3 for malignant WHO grade III meningiomas. Moreover, there is also a subtype connection between the ICD-Oncology and the WHO CNS *e.g.* 9537/0 for transitional meningioma. However, unlike the CCAM which enables to know the precise site of the tumour origin, the ICD oncology like the ICD-10 includes only two topographic codes: cerebral *vs.* spinal meninges. Therefore, the ICD-O is accurate for the grading but, not for the location. Yet, the PMSI database does not deal with the ICD-O. We suggest to integrate the use of ICD-O within the PMSI database and, to change the ICD-10 classification by making each of the three ICD-10 codes correspond with the three grades of meningioma defined in the WHO CNS 2016 classification. For example, D42 "Neoplasm of uncertain or unknown behaviour of meninges" should be strictly specified as "WHO grade II" as we hypothesise in our method.

4.7. Tumour location

One of the advantages of the PMSI database which use the CCAM classification is to provide the precise location of the tumour insertion on the dura mater. Without surprise, meningiomas of the convexity are the most common. Data on spinal meningiomas epidemiology have rarely been reported. We found a proportion of 9.84% and an incidence of 0.44 compare to 0.32/100 000 for the US registry [25].

Despite the likely flaw in grading distribution, we have found a slight but significant over-representation of aggressive tumours of the "convexity area" compared to the skull base. This difference was previously noticed and explained through genetic alterations. Clark et al. showed that the mutational profile of a meningioma can largely be predicted based on its anatomical position *id est* meningiomas with mutant NF2 and/or chromosome 22 loss were more likely to be atypical - grade II and localised to the cerebral and cerebellar hemispheres.

4.8. Geographical variation

There are departmental variations of benign, uncertain and malignant meningiomas incidences. Areas of high *vs.* low incidences can be spotted without any regular pattern or meaningful organisation. The PMSI allows to easily study the geographical distribution of meningioma or others neoplasms, which can be informative for clinicians. There are notable variations of incidences. Though, we have to be mindful that malignant or uncertain behaviour meningiomas are rare tumours and several departments count none or only one case over 9 years. Therefore, such an unequal distribution of small numbers is likely to some extent, the result of chance and should be regarded with caution. For benign meningiomas, department incidences vary from 2.09 to 5.88. This is surely the result of a complex multi-factorial explanation including *e.g.* environmental, probabilistic and also local medical practices. To our knowledge, no study has ever investigated the spatial distribution of meningioma within a country.

5. Conclusion

The PMSI database is a reliable and effective source for studying the epidemiology of meningiomas, including the precise location of the tumour. Our findings comfort previous studies and are comparatively correlated. This may assert the usefulness of such a database to investigate the patients' outcome.

Conflict of interest

None. We authors, Charles Champeaux, Joconde Weller, Sandrine Katsahian declare to have no personal, financial or institutional interest in any of the drugs, materials, or devices described in this article. We report no declarations of interest. We are responsible for the content and writing of the paper.

Compliance with ethical standards

This study was conducted according to the ethical guidelines for epidemiological research in accordance with the ethical standards of the Helsinki Declaration (2008) and the French data protection authority (CNIL).

Authorship contribution

Charles Champeaux: conception and design, acquisition of data, analysis and interpretation of data; drafting the article and revising it critically for important intellectual content, final approval of the version to be published.

Joconde Weller: conception and design, acquisition of data, analysis and interpretation of data; drafting the article and revising it critically for important intellectual content, final approval of the version to be published.

Sandrine Katsahian: conception and design, final approval of the version to be published.

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Appendix A. Supplementary data

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