Magnetoencephalography (MEG) versus magnetic resonance imaging (MRI) for diagnosis of pediatric epilepsy.

ABSTRACT - Background: Magnetoencephalography (MEG) and magnetic resonance imaging (MRI) are two imaging modalities commonly used to assess patients with epilepsy. Although they have been extensively compared in adults, there is a lack of comparative studies in pediatric epilepsy.

Methods: Twenty children (10 males and 10 females) with epilepsy and a mean age of 12.5 years were included in the study. All patients underwent MEG and MRI. The MEG data were analyzed using a commercially available software and the MRI images were analyzed by two neuroradiologists.

Results: The MEG data showed a significant increase in the number of spikes and interictal spikes in the right hemisphere in 15 patients. MRI showed structural abnormalities in the brain in 12 patients, including cortical and subcortical lesions.

Conclusions: The results of this study suggest that MEG and MRI have complementary roles in the diagnosis of pediatric epilepsy. MEG can provide more detailed information about the location and extent of the epileptogenic tissue, while MRI can provide information about the underlying structural abnormalities.

How to cite this article: Magnetoencephalography (MEG) versus magnetic resonance imaging (MRI) for diagnosis of pediatric epilepsy. ABCD Arq Bras Cir Dig. 2019;32(4):e1471. DOI: /10.1590/0102-672020190001e1471
INTRODUCTION

The increased use of computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasonography (EUS) has increased the recognition of pancreatic cystic lesions, classified as neoplastic and pseudocysty. The most common cystic neoplasms are: serous cystic neoplasia, mucinous, solid-cystic pseudopapillary, and papilliferous mucinous mucinous intraductal neoplasia (NIMP). The diagnosis and treatment of the latter has evolved since its first description by Ohashi et al. It is a precursor of pancreatic cancer and has mucin-producing epithelium, which develops preferentially within the main pancreatic duct and has been increasingly diagnosed.

Because these lesions vary in type and extent, the ideal examination for adequate characterization needs to be sensitive enough to provide faithful images of extent of damage. In addition, it should provide specific and accurate evaluation in order to establish the differential diagnosis between NIMP and cystic mucinous neoplasia. Despite the development of imaging methods, there is still no ideal method for studying this disease. Regarding CT and MRCP, current literature is limited to demonstrate its diagnostic accuracy, as well as to assess the involvement and size of the main pancreatic duct. CT is used for diagnosis and initial characterization in patients with NIMP but its use as a single source of images before surgery is common. Waters et al. believe that CT alone may not be sufficient to establish the diagnosis and accurately determine tumor type and extent, requiring MRCP for complementary analysis. It is observed that the use of other diagnostic methods has been necessary. Endoscopic retrograde cholangiopancreatography, endoscopic ultrasonography (mini-probe) and conventional echoendoscopy are invasive methods that can be used with doubtless success for diagnosis.

Echoendoscopy evaluates the type and extent of NIMP, but according to Waters et al. have blind spots, unable to accurately determine the extent and involvement required for preoperative planning. In addition, it is not widely available method, even in the USA. Contrary to what these authors define, the experience of the present paper has been rewarding. One of the key points is, in addition to allowing the classification and analysis of type and extension, that it provides for the possibility of surgical resection and for obtaining material to characterize the degree of cellular atypia, and assess the possibility of surgical resection.

MRCP, unlike the echocardiop ductal puncture, is non-invasive and allows evaluation of the pancreatic duct, providing the same information in the identification of nodules, vegetations, but cannot simultaneously collect material for anatomopathological evaluation.

The objective of this study was to compare the EPAAF with the results obtained by MRCP in the diagnosis and extension of proven NIMP after surgical resection.

METHODS

This study was carried out at the Department of Endoscopy of the 9 de Julho Hospital, São Paulo, SP, Brazil, and at the Institute of Medical Research of the Evangelical Faculty of Paraná, Curitiba PR, Brazil, approved by the Institutional Ethics Committee under number 53037816.0.0000.0103

Inclusion and exclusion criteria

Only those who had been diagnosed with NIMP - both during EPAAF and MRCP - and operated with resected material sent for histological analyses, were included.

Patient selection and surgical procedure

Thirty-six patients submitted to surgical resection with preoperative suspicion of NIMP were selected and studied. The data were collected from a prospective database, obtained from the date when the patients had clinical suspicion of NIMP by the imaging tests. All were sent to EPAAF, with the purpose of histological diagnosis and confirmation of NIMP.

The data of both for each patient were recorded focusing: 1) correct diagnosis of the lesion; 2) classification main duct (type I), secondary duct (type II) and mixed (type III); 3) nodules or vegetation; 4) focal disease (a single segment of the pancreas) or multifocal (more than one segment); and 5) place of attachment and extension (head, body and tail).

Twenty-one men and 15 women were enrolled. The mean age at the time of the operation was 62.4 years (11-89). Sixteen were submitted to duodenopancreatectomy, 16 to subtotal pancreatectomy, and four to exploratory laparotomy, because they presented non-resectable tumor (Table 1). The operation was performed in all selected patients, with standardized mean time of three months after puncture.

TABLE 1 - Demographic aspects and type of surgical treatment imposed on patients with suspected NIMP

| Parameters | n   | Age, years (range) | Gender |
|------------|-----|--------------------|--------|
| Age        | 62.4 (11-89) |
| Gender     |     |
| Female     | 21  |
| Male       | 15  |
| Procedure  |     |
| Duodenopancreatectomy | 16 |
| Subtotal pancreatectomy | 16 |
| Exploratory laparotomy | 4 |

Equipment

All EPAAF exams were performed by the same gastroenterologist (JCA) with over 25 years’ experience in diagnostic and therapeutic EUS. We used the Fujifilm ultrasonic platform model SU 7000 and the sectoral echoendoscopic model EG 530UT.

Parameters evaluated

Images obtained by both methods were analyzed using a standardized list containing the type and classification of the lesion; anatomical localization of the main cyst (head, body and tail); focal and multifocal distribution; existence of communication between cystic lesion and the main pancreatic duct; and identification of nodules and/or vegetation within the cyst or attached to its wall.

Thus, involvement of the main duct was considered when exams showed diameter greater than 0.9 cm in one segment or filling faults inside the duct. All these aspects were considered as additional factors for the diagnostic involvement of the main duct.

Classification

When the methods identified dilatations of the main pancreatic duct, it was classified as injury of main duct or type I; the involvement of the secondary ducts individually
Afterwards, the instillation of physiological solution in the inflated for progression of the device to the second duodenal and progression blindly to the esophagus, due to the oblique vision until the transposition of the cricopharyngeal muscle for the examination. Patients always remained in the left lateral decubitus and anticholinergic agents to decrease duodenal motility as needed. Patients always remained in the left lateral decubitus for the examination.

The pathological examination revealed 33 patients with NIMP. Twenty-nine had a non-invasive type, 16 adenomas, 10 borderline, and three as in situ carcinomas. Four presented the invasive form. The other three were diagnosed as intraepithelial neoplasia (NIPan grade 2, Table 2). Two patients were classified as grade 2 NIPan, high grade or carcinoma “in situ” and invasive. Two patients were re-established, he was discharged with a prescription of Ciprofloxacin 500 mg orally every 12 h for five days.

**RESULTS**

**Pathological, surgical and classification findings**

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**TABLE 2** - Pathological aspects of NIMP (n=33) and NIPan (n=3)
Parameters | n
--- | ---
Anatomopathological (NIMP) | 
Adenoma | 16
Borderline | 10
Carcinoma in situ | 3
Invasive | 4
Pathological classification (NIPan) | 
Grade 2 | 3

Twenty-five had involvement in the main pancreatic duct, three of the secondary duct, and eight of the mixed type. Pathological and surgical findings revealed that the lesion was focal in 28 and multifocal in eight. In 21 the results demonstrated the presence of nodules and/or vegetations being adenocarcinoma “in situ” (n=4) and adenoma (n=17). According to the surgical findings and/or pathological lesion, a head injury was demonstrated in 21, in more than one segment in eight and body seven. Of the three patients with type II suspected EUS, all had type 2 NIPan without nodules and/or vegetations (Table 3).

The mean size of the larger cystic lesions was 3.7 cm (0.9-10.5). Twenty-one patients had cystic lesions smaller than 3 cm; five between 3.1 and 5.0 cm and 10 greater than 5 cm.

### TABLE 3 - NIMP classification

| Classification | Pathology | MRCP | EUS | p  |
| --- | --- | --- | --- | --- |
| a) Types of NIMP | 
Main duct (I) | 25 | 21 | 25 | 0.811
Mixed (III) | 8 | 5 | 6 | 1
Secondary pipeline (II) | 3* | 1 | 3 | 1 |
| b) Focal or multifocal | 
Focal | 28 | 20 | 27 | 0.638
Multifocal | 8 | 5 | 6 | 1 |
| c) Nodules and vegetation | 
Gift | 21 | 10 | 19 | 0.5
Absent | 15 | 15 | 15 | 1 |
| d) Location of the lesion | 
Head | 21 | 17 | 19 | 1
More than one segment | 8 | 5 | 7 | 1
Body | 7 | 3 | 7 | 1 |

* = Two cases of pancreatic intraepithelial neoplasia

**Magnetic resonance cholangiopancreatography**

The diagnostic suspicion was NIMP in 27/36 (75.4%), mucinous cystadenoma in 5/36 (13.8%), serous cystadenoma 3/36 (8.1%), cystadenocarcinoma in 1/36 (2.7%). The correct diagnosis of type I, II and III, occurred in 100%, 100% and 75%, respectively and correctly showed a focal lesion in 27/28 (96.4%) and multifocal lesion in 6/8 (75%).

**Ecoendoscopy associated with fine needle puncture**

The diagnostic suspicion of NIMP occurred in 27/36 (75%), mucinous cystadenoma in 5/36 (13.8%), serous cystadenoma 3/36 (8.1%), cystadenocarcinoma in 1/36 (2.7%). The correct diagnosis of type I, II and III, occurred in 100%, 100% and 75%, respectively and correctly showed a focal lesion in 27/28 (96.4%) and multifocal lesion in 6/8 (75%).

**Comparison between EPAAF and MRCP for diagnosis and classification of NIMP**

The ROC curve demonstrated that EUS revealed better accuracy when compared to MRCP, but the test were invalidity: its results were no better than chance. EUS presented greater sensitivity and specificity when compared to MRCP in the identification and classification of nodules and/or vegetations within the cystic areas of NIMPs (Figure 5).
Furthermore, in the present study, three cases identified as larger in relation to the mixed type and practically non-existent has major implications for the stratification of patients who are described. The correct classification of the pathological type identification of the dilatation of the main pancreatic duct from the radiological point of view, the diagnosis is made through the clinic is based on history, endoscopic findings, cytology and, in some cases, obtaining a sample for pathological examination. Each image of the contrast study of the ducts of both regions is studied by medical specialists in radiology and gastroenterology, to compare the results of the operation with pathological findings. The entire study followed standardized criteria, because this disease can evolve over time and change its type and size. Therefore, the patients underwent surgical treatment within three months after the analysis by these imaging exams. According to this study, both are excellent methods for the determination of risk of developing pancreatic cancer and to determine the best treatment in an individualized way.

DISCUSSION

The diagnosis and treatment of NIMP remains controversial. With the quality and availability of current imaging studies, in addition to a better understanding of physicians, the disease has been increasingly diagnosed. Thus, it is important for the surgeon to apply the best possible diagnostic method through imaging tests available in clinical practice to accurately determine the diagnosis, characterization, extent, and type of tumor. These factors have important implications, especially in the elderly with comorbidities, to establish a correct stratification of the risk of developing pancreatic cancer and to determine the best treatment in an individualized way.

This study was performed in patients who had a strong suspicion of NIMP by MRCP. All patients were referred for echocardiographic puncture and then confirmed the results by obtaining a sample for pathological examination. Each image was carefully studied and the main information was recorded by medical specialists in radiology and gastroenterology, to compare the results of the operation with pathological findings. The entire study followed standardized criteria, because this disease can evolve over time and change its type and size. Therefore, the patients underwent surgical treatment within three months after the analysis by these imaging exams. According to this study, both are excellent methods for the diagnosis and classification of this neoplasm with similar results. However, echocardiographic puncture has advantages over MRCP, which are: 1) precise diagnosis of the degree of cellular atypia; 2) precise determination of nodules and/or vegetation; 3) identification of the extent of the disease. These data corroborate with Martin’s study.

The diagnosis of NIMP can be clinical or pathological. The clinic is based on history, endoscopic findings, cytology obtained by endoscopy, and radiological findings. From the radiological point of view, the diagnosis is made through the identification of the dilatation of the main pancreatic duct described. The correct classification of the pathological type has major implications for the stratification of patients who are at risk of developing pancreatic cancer. Knowledge of this fact also determines the best treatment for them.

The malignant potential involving NIMP of the main duct is larger in relation to the mixed type and practically non-existent when it affects the secondary duct. Thus, involvement of only the secondary duct provides a lower risk of pancreatic cancer. Furthermore, in the present study, three cases identified as type II NIMP in the imaging were not confirmed as such, but as grade 2 pancreatic intraepithelial neoplasia, accompanied by dilation of secondary ducts. This finding is similar to that described by other authors. It is noteworthy that in this study the puncture suspected NiPan in two cases, while the images obtained by MRCP and the EUS of type II NIMP with small dilatation of the main duct.

Dilation of the main duct as an isolated tumor component may be the most important radiographic criterion of high risk for invasive cancer or risk of malignancy. Thus, in this study, both were effective in classifying the type correctly. This is especially true in patients with comorbidities and low-risk lesions who could have their tumor controlled through periodic follow-up instead of receiving surgical treatment.

The extent of the disease also has significant implications, both for the stratification of cancer risk and for making the right decision on surgical resection margins, in order to prevent relapse. In addition, new evidence suggests that mixed-type multifocality is associated with malignancy. Although MRCP is sensitive to detect small lesions on secondary ducts, it presented inferior results when compared to the EPAAF to identify lesions smaller than 0.5 cm.

The rate of relapse after surgical resection may be influenced by the sensitivity in detecting the extent of the disease in the preoperative period. In this study, there were only two recurrences after the Whipple procedure identified by MRCP and confirmed by the EPAAF, requiring total pancreatotomy of the remaining gland. Another point to be discussed is that this may give a false idea of a high rate of recurrence due to a miscalculation in the extent of preoperative disease, when in fact the lesions were too small to be recognized in imaging tests. This aspect opens the door to new clinical research where the use would be part of the research by absorbing patients with suspected disease, as it can, with high accuracy, identify tiny cystic areas not seen by other methods.

The guidelines of this consensus on mucinous cystic neoplasm and NIMP state that MRCP is the best method to describe the appearance of lesions and is useful for determining communication with the ductal system. This study demonstrates that, in addition to EUS to determine results similar to other methods to evaluate these parameters, it also more accurately identifies the presence of nodules and vegetations (predictors of malignancy) and presents a sensitivity rate of 80% for histological and clinical diagnosis. This international consensus suggests that mucinous cystadenoma should be resected and asymptomatic patients with type II NIMP smaller than 3 cm can be observed safely. In addition, it also determines that MRCP is equivalent to CT for investigation of pancreas looking for small secondary ducts.

Based on this careful selection of patients with the disease and data analysis, it seems clear that MRCP has a high resolution for the planning and adoption of therapeutic measures, but in addition, the preoperative propaedeutics by EPAAF becomes useful, due to the high sensitivity to detect nodules/vegetations, besides confirming the diagnosis of malignancy (sensitivity of 80% of the puncture). Previous studies have not adequately addressed this issue, targeting the best modality for NIMP management, and no published study comparing these diagnostic methods was found. They are found in the literature evaluating several isolated imaging methods. However, Kawamoto et al. justifies that there is no indication for puncture due to the existence of blind spots in the echoendoscopy, in addition to not assessing the extent of the disease satisfactorily. However, the opposite was demonstrated, being effective to identify the type (I, II and III), multifocality and, even better if compared to MRCP to show nodules or vegetations, in absolute numbers, in addition to a better understanding of physicians, the disease could have its tumor controlled through periodic follow-up instead of receiving surgical treatment.

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Sahani et al. demonstrated CT and MRCP accuracy to assess the involvement of the main duct. They demonstrated...
their sensitivity to identify the communication between the cystic lesion and the main pancreatic duct. The sensitivity found was 63% and 67%, respectively. In addition, the diagnostic performance of CT and MRCP to determine the malignant potential of NIMP was similar and agreed, suggesting that follow-up with both modalities can be used.10

The international consensus guidelines for pancreatic cystic lesions report that the diameter of the main duct greater than 1 cm strongly suggests this disease.13 Signs of chronic pancreatitis occurred in many patients, evidenced by tortuosity and dilation of the main duct. In addition, the presence of mucin plugs downstream may result in obstruction and dilatation thereof upstream. Any of these factors can lead to misclassification and overestimate the diagnosis. To avoid this problem, the authors indicated the echo-guided puncture to confirm the diagnosis by obtaining fragments of dilated main duct. There is no doubt about the accuracy of these diagnostic modalities to determine the diameter, but the images provided even for one segment, the latter through the eco-guided puncture, allow better characterization as evidenced by its similarity with findings from pathological studies. In the data of this series related to ductal communication, they were based on the radiological and ultrasonographic analysis performed before the histological diagnosis. Thus, it can be observed that the results of both were similar.

EUS is considered the gold standard examination for pancreatic investigation, providing data on the morphology of these lesions and enabling, through real-time fine needle guided puncture, the collection of material for histological evaluation and tumor biochemical markers. It is known that NIMP has malignant potential and malignancy indications are: pancreatic duct involvement, dilatation above 5 mm, cystic cavity greater than 30 mm, presence of mucine nodules, existence of a tissue component developed at from a cystic lesion and the presence of lymph nodes. Complete resection is recommended, especially for the main duct NIMP, and especially in the presence of symptoms. The risk of malignancy of secondary ductal NIMP is lower, suggesting that surveillance may be sufficient to avoid functional loss of the pancreas associated with surgical resection.10 Increasing efforts have been made to identify predictors of malignancy and avoid indications of unnecessary secondary ductal NIMP surgical resection, resulting in a second set of recommendations from the international consensus guidelines, the Fukuoka International Consensus, published in 2012.

The guidelines of this consensus on mucinous cystic neoplasia and NIMP state that MRCP is the best method to describe the appearance of lesions and is useful for determining communication with the ductal system.3,4 This study demonstrates that, in addition to EUS to determine results similar to other methods to evaluate these parameters, it also more accurately identifies the presence of nodules and vegetations (predictors of malignancy) and presents a sensitivity rate of 80% for histological diagnosis. This international consensus suggests that mucinous cystadenoma should be resected and asymptomatic patients with type II NIMP smaller than 3 cm can be observed safely. In addition, it also determines that MRCP is equivalent to CT for investigation of pancreas looking for small secondary ducts of small proportions.3,9 These guidelines, however, do not directly address the best imaging modality to be used preoperatively for accuracy of diagnosis, type and extent of disease. In addition, it cannot be forgotten that three patients with type II suspicion (with lesions smaller than 3.0 cm) were diagnosed with NIPan and according to the guidelines these patients should be followed by imaging. Thus, in view of the importance of a correct follow-up for NIMP, its validation may generate new studies,11 encouraging the greater applicability of the EAPAF for the diagnosis and follow-up of these pancreatic cystic neoplasms.

CONCLUSION

Both studied methods did not have significant statistical difference for the diagnosis and determination of the extent of NIMP. However, the EAPAF revealed better absolute results to identify nodules and/or vegetations, besides providing histological diagnosis and being essential for the management of the disease.

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