Review on Factors Affecting Diagnostic Yield in Stereotactic Biopsy for Brain Lesions: A 5-Year Single-Center Series.

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Research Article

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Abstract

Objective: To determine the factors that are associated with the diagnostic yield of stereotactic brain biopsy.

Materials and Methods: A retrospective analysis was performed on 50 consecutive patients who underwent stereotactic brain biopsies in a single institute from 2014 to 2019. Variables including age, gender, lesion topography and characteristics, biopsy methods and surgeon's experience were analyzed along with diagnostic rate.

Results: This study included 31 male and 19 female patients with a mean age of 48.4 (range: 1-76). Of these, 25 underwent frameless brain-suite stereotactic biopsies, 15 were frameless portable Brain-lab® stereotactic biopsies and 10 were frame-based CRW® stereotactic biopsies. There was no statistical difference between the diagnostic yield of the three methods. The diagnostic yield in our series was 76%. Age, gender and biopsy methods had no impact on diagnostic yield. Periventricular and pineal lesion biopsies were significantly associated with negative diagnostic yield ($p=0.01$) whereas larger lesions were significantly associated with a positive yield ($p=0.01$) with the mean volume of lesions in the positive yield group (13.6cc) being higher than the negative yield group (7cc). The diagnostic yields seen between senior and junior neurosurgeons in the biopsy procedure were 95% and 63% respectively ($p=0.02$).

Conclusion: Anatomical location of the lesion, volume of the lesion and experience of the surgeon have significant impacts on the diagnostic yield in stereotactic brain biopsy. There was no statistical difference between the diagnostic yield of the three methods, age, gender and depth of lesion.

Introduction

The diagnosis of an intracranial lesion remains challenging if based solely on clinical and radiological presentation as it may be incorrect in one third of patients. [2,20] Hence, histological diagnosis plays a crucial role in guiding treatment strategies. For many decades, stereotactic brain biopsy techniques have been widely utilized to obtain tissue from the brain for histological diagnosis. [2,15,20]

The current stereotactic brain biopsy is divided into frame-based and frameless method. The results from a meta-analysis suggested no significant difference exist between frame-based and frameless biopsy method in the terms of diagnostic yield, morbidity, and mortality. A diagnostic yield of more than 85% is generally acceptable. [4] There are various factors that have been reported which affect diagnostic yield in stereotactic needle biopsy for brain lesions. They include age of the patient, gender, lesion's volume, histology and location of the brain lesion. [3,19]

In our hospital, the stereotactic biopsies were guided and carried out by neurosurgeons with different seniority of experience. The objective of our study is to review the cases at our institution in order to determine the predictive factors associated with positive diagnostic yield in stereotactic biopsy.

Materials And Methods

Study Design and Patient Population

We performed a retrospective study of all consecutive patients who underwent stereotactic biopsy for intracranial lesion in our institution from 2014 to 2019. The study setting was in a single tertiary center, which covers a population area of 2.7 million. The decision for brain biopsy was made by the attending neurosurgeon involved in each individual case. The number of patients who underwent stereotactic brain biopsy determined the study size. Some patients underwent more than one biopsy due to negative diagnostic yield during the first biopsy. These subsequent biopsies were not included into the analysis. This study was approved by the institute review committee of the hospital.

Biopsy Technique

In our hospital, patients underwent brain biopsies with 3 different types of biopsy system: Portable Brain-lab Vector Vision®, Brain-suite Brain-lab Curve® and Cosman-Roberts-Wells (CRW)® stereotactic frame. All biopsies were planned and performed by the in-charged neurosurgeon and the choice of system was based on individual preference.

For the frameless biopsy, head MRI was performed before the operative day without fiducials, and the images were transferred to the neuronavigational system (Brain-lab). The planning of the biopsy including the optimal entry point, target and trajectories were done prior to the day of biopsy. On the day of biopsy, patient's head was immobilized in a Mayfield head clamp and navigation system registration was done. Surface registration was used for Portable Brain-lab Vector Vision® while intraoperative Computed Tomography (iCT) registration was used for Brain-suite Brain-lab Curve®. After confirming the accuracy of the neuronavigational system, a burr-hole was placed at the intended entry point. With the assistance of Varioguide Biopsy instruments, the biopsy samples were obtained using Brain-lab® biopsy needle.

For the frame-based biopsy, the CRW® frame was used in all cases. Head MRI was performed similar as the frameless biopsy group. MRI images were transferred and reviewed with OsiriX®. By using the OsiriX® MPR curve, the optimal entry point, target and trajectories were chosen. On the operative day, neurosurgeons fixed the CRW® stereotactic frame on the head of the patient, using local anesthesia. A computed tomography (CT) scan was performed with the frame and the localizer in place. Radionic Stereocalc® was used for image registration, targeting, and calculation of offsets, ring and arc settings. The arc system was set up and attached to head ring in sterile environment. A burr hole was placed at the intended entry point, and biopsy samples were obtained using Nashold® needle.

On average, 4 biopsy specimens were obtained either through a single trajectory or multiple trajectories if needed. There was no frozen section service available in our institute. All specimens were sent to histopathology lab for definitive histological examination by pathologists. An early post-biopsy CT

imaging will be performed to look for air bubble within the lesion's target which indicates radiological accuracy and at the same time to look for any intracranial bleeding.

Clinical and Radiological data

The demographics, clinical and histology results were collected from medical records. Brain imaging were reviewed in a computer (OsiriX®) or printed films. From these data, we retrospectively collected age, gender, images characteristics, biopsy techniques, surgeon's experience, duration of surgery and post-surgery complications. The diagnosis was obtained from the final histopathological or culture reports.

Statistical Analysis

Descriptive analysis was conducted to describe the profile, clinical characteristics and diagnostic yield of the stereotactic brain biopsies. Exploratory data analysis was initially performed to assess the relationship between the variables and descriptive statistics. Odds ratio, Chi-square, Independent sample T-Test and 95% Confidence-Interval ratios were calculated. P values of < 0.05 were regarded as statistically significant. These data were tabulated in Microsoft Excel © and further analyzed using SPSS software version 20.0 ® (SPSS Inc., Chicago, IL.).

Results

A total of 50 patients, 19 females and 31 males, were included into the study. Ages ranged from 1 to 76 years with a mean of 48.4 years. In our series, although 88% of the cases shown radiological evidence of accuracy in the post-biopsy CT imaging, the positive diagnostic yield was only 76% (38/50), with 12 inconclusive results. Post-procedural permanent morbidity was 4%, mainly due to the bleeding over the biopsy site. There was no mortality in this study. Table 1 and 2 depict the data of the study and comparison of positive and negative diagnostic yield respectively.

Demographics

Patient's age was not associated with the diagnostic rate as the mean age of positive and negative diagnostic yield group was 48.6 years and 47.4 years respectively ($p=0.85$). Similarly, the gender of the patients was not associated with the diagnostic rate, as negative biopsies occurred in 3 female and 9 male patients ($p=0.33$).

Lesion's topography and characteristics

All the biopsied lesions were contrast enhanced. The other characteristics of the lesion includes its volume and anatomical location. Lesions' volume ranged from 1cc to 67cc (mean: 15cc). By comparing the mean volume of the positive (13.6cc) and negative (7cc) diagnostic yield group, it showed a statistically significant difference between the two groups demonstrating the influence of the bigger lesions on clinching a definite diagnosis ($p=0.01$). For the 6 cases with lesion's volume 1cc and less, the

diagnostic yield was 50%. When we include the total 11 cases with lesion's volume 2cc and less, the diagnostic yield was 54.5%. As for the location of the lesion, there is no difference of diagnostic rate between the deep and superficial located lesions. However, a subgroup analysis on the pineal and periventricular lesions, showed 5 out of 6 biopsies turned out to have negative diagnostic yield (Figure 1), ($p=0.01$).

Biopsy methods

Twenty-five biopsies were frameless brain-suite stereotactic, fifteen were frameless portable Brain-lab® stereotactic and ten were frame-based CRW® stereotactic. There was no statistical difference between the diagnostic yield of the three methods (Table 3). The mean duration of frame based CRW® stereotactic biopsy was the shortest compared to the other two. This was 60.5 minutes, which statistically significant when compared to brain-suite biopsy in saving operative time ($p=0.04$).

Diagnostic yield negative cases

There were 12 negative diagnostic yields. 4 cases underwent second stereotactic biopsies, and 2 cases underwent open biopsies which managed to establish histological diagnosis. The other 6 patients did not manage to undergo re-biopsy which 4 of these patients defaulted treatment and 2 patients were treated empirically with steroids (Figure 2).

Surgeon's experience

In our institute, stereotactic biopsies are guided and carried up by multiple neurosurgeons with difference level of experience in the field of stereotactic biopsy. We divided the neurosurgeons into 2 groups based on number of stereotactic biopsies performed previously by the neurosurgeons.

- Group 1 (Senior Level): Neurosurgeon who had performed 20 cases and more stereotactic biopsies.
- Group 2 (Junior Level): Neurosurgeon who had performed less than 20 cases stereotactic biopsies.

Twenty biopsies were conducted by Group 1 and thirty biopsies by Group 2. The diagnostic yields were 95% and 63% respectively (Figure 3). This showed that more experienced surgeon was a significant predictive factor for positive diagnostic yield ($p=0.02$). We did not find a significant difference in the demographics, lesion's topography and characteristics, and biopsy methods between the two groups (Table 4). As mentioned earlier, the smaller lesions (1cc and less, 2cc and less) gave significant low diagnostic yields. However, when we sub-analysed these, we discover that the group 1 did provide a higher diagnostic yield even in the small lesions biopsy which are 75% (3/4) and 100% (3/3) for lesions 1cc and less, and 1-2cc respectively. Besides, with subsequent involvement and guidance of a senior, experienced neurosurgeon, all the 4 re-biopsy cases managed to produce positive diagnostic yield in the second stereotactic biopsy individually performed by the junior neurosurgeon.

Discussion

Demographics

In our series similar to most studies, [6-9] age and gender of the patient did not correlate with the diagnostic yield, despite some authors reporting that biopsies in the older patients were more likely to result in a definite diagnosis than in a younger patient and a negative influence of the female gender. [5,10,11] In one study where the author uses the age of 40 years as an arbitrary cut-off point, younger patients (<40 years old) had a diagnostic yield of 75.9%, whereas older patients (>40 years old) had a diagnostic yield of 90.6%. [14]

Lesion's topography and characteristics

The depth of the lesion does not affect the diagnostic yield in our series. This is similar to the others who also reported that lesion depth does not influence success rate in stereotactic biopsy. [5,19] However, there is a study which reported significantly greater negative diagnostic yield in biopsies of deep-seated lesions. [13] Anatomical location of the lesion was found to be a significant factor for positive diagnostic yield in some studies [1,9,19,21] and not in others. [6,7,10,16,18] In our series, we found that lesions which were located at the periventricular and pineal region were significant associated with a negative diagnostic yield. This is due to the high incidence of biopsy needle penetration into the cistern or ventricle causing cerebral spinal fluid aspiration during tissue sampling. This loss of negative suction pressure causes loss of tissue catch into the biopsy needle aperture. Thus, a tissue sampling error happens.

The volume of the lesion was reported as one of the factors influencing the diagnostic yield in stereotactic biopsy. [11,21] The smaller the lesion, the greater the likelihood obtaining a negative diagnostic yield and vice versa. Similar results were observed in our series. However, some authors reported size did not matter. [6,16] In our series, the preference of using CRW® frame stereotactic biopsy in smaller lesion is evidenced by the smaller mean volume of lesion of 8cc as compared to frameless brain-suite (12.5cc) and portable Brain-lab® (14cc) stereotactic biopsy. In general, it is recommended to employ frame-based techniques for small lesions in order to minimize the sampling error. [16,17,19,22]

Biopsy methods

Historically, frame-based technique had been labelled as gold standard in stereotactic biopsy. A recent meta-analysis showed no differences in terms of diagnostic yield and complication between frame-based and frameless stereotactic biopsy. [4] In our series, we also demonstrate no significant difference in diagnostic yield between the diagnostic yield of the three methods. The main advantage of frame-based technique is shorter operating theater time compared to the frameless technique. Similar findings were reported by other authors as well. [3]

Surgeon's experience

Up to date, there is no literature discussing surgeon's experience as one of the factors that may influence the diagnostic yield in stereotactic brain biopsy. From our series, we found significant difference

between senior and junior neurosurgeon who guided and performed the stereotactic biopsies. The Group 1 (Senior level) neurosurgeons managed to achieve higher positive diagnostic yield (95%). This group also achieved 100% radiological accuracy compared to 80% by the Group 2 (Junior level) neurosurgeons. We speculate that guidance and involvement by senior, experienced neurosurgeons were associated with higher accuracy and positive diagnostic yield. They had more experience in pre-biopsy planning including target, entry and trajectory selection, more familiarity with the biopsy system and every steps of the biopsy procedure. Stereotactic surgery demands meticulous attention to detail during every step of the procedure. [23] Variance in neurosurgeons' proficiency and expertise in performing stereotactic surgery like deep brain stimulation electrode implantation among different institutions/hospitals had been reported as a significant contributor to the accuracy. [12] Further analysis had ruled out bias between the 2 groups in term of patient's demographics, lesion's topography and characteristics, and biopsy methods. In addition, most of the smaller lesion's biopsies were performed under the senior, experienced neurosurgeons and delivered an acceptable diagnostic yield as mentioned earlier. For the 4 stereotactic re-biopsy cases, all subsequently manage to produce positive diagnostic yield in second biopsy by the help of a senior, experienced neurosurgeon. Guidance and involvement by a senior, experienced neurosurgeon in stereotactic biopsy is definitely helpful in obtaining a positive diagnostic yield and hasten the junior neurosurgeon's learning curve in stereotactic biopsy procedures.

Limitations of the study

The main limitation of this study is that its non-randomized and single center. Furthermore, the number of biopsy cases is relatively low when compared to other biopsy series. Another limitation that might affect the diagnostic yield and results was the fact that several pathologists were involved with the assessment of the biopsy specimens. Even though that happened randomly, it could have been a confounding factor. There was no frozen section available in this series due to unavailability.

Strengths of the study

We have presented a real-life series involving neurosurgeons of various experience levels, which is reflective of routine practice and analyzed the factors influencing the diagnostic yield. This is probably the first published series reporting on the surgeon's experience as one of the critically important but underreported factors influencing the diagnostic yield in stereotactic brain biopsy.

Conclusion

This study shows anatomical location of the lesion, volume of the lesion and experience of the surgeon as independent variables that influence diagnostic yield in stereotactic brain biopsy. Age, gender, biopsy method and depth of lesion showed no statistical relationship.

Declarations

Funding Sources

This study did not receive any funding or financial support.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Data Availability Statement

The data that support the findings of this study are not publicly available on legal or ethical grounds except an approval from Hospital director.

Code Availability and Material

Not applicable.

Ethics Approval

This study was approved by the Medical Review & Ethics Committee (MREC), Ministry of Health Malaysia. The research ID is 60517. The study complies with the guidelines for human studies and conducted ethically in accordance with World Medical Association Declaration of Helsinki. This is a retrospective data collection study.

Consent to participate

Not applicable

Consent for publication

A hospital director's consent was granted for data collection. Director's consent for publication was granted as well.

Author Contributions

Conception and design: Bik Liang Lau. Acquisition of data: Bik Liang Lau, Kugan Vijian. Analysis and interpretation of data: Bik Liang Lau, Kugan Vijian. Drafting the article: Bik Liang Lau. Critically reviewing the Article: Bik Liang Lau, Albert Sii Hieng Wong. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Bik Liang Lau. Administrative / technical / material support: all authors. Agreement to be accountable for all aspects of work: Bik Liang Lau

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Tables

Due to technical limitations, table 1-4 is only available as a download in the Supplemental Files section.

Figures

Figure 1

Summary of diagnostic yield in relationship to anatomical location of the intracranial lesion.

Figure 2

The sequela of the cases with negative diagnostic yield after the first stereotactic brain biopsy.

Figure 3

The diagnostic yield of stereotactic biopsy between case with consultant (Exp > 5 years) and non-consultant (Exp < 5years) involvement.

Supplementary Files

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