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Teaching practical histopathology during COVID-19 pandemic: A remote education model for students

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Abstract: Objectives: Unfortunately, COVID-19 pandemic has limited physical activities, leading to shut education faculties, including clinical clerkships for medical students. This compromises particularly interactive learning such as pathology education and science researching.
The present study aims to describe a remote, fast, low-cost and reproducible learning method for histological score application and pathology learning in students.
Methods: Eight medical students with no previous training in histopathology were instructed online in a two-step learning process consisting in a first stage of streaming self-regulating learning and a second stage of computer assisted instruction using animated samples. Every student analyzed twice 32 histological samples of liver in different degrees of ischemic damage using a proposed score and a gold standard score. These results were compared to the ones obtained by two experts in pathology using intraclass correlation coefficient.
Results: Intra class correlation coefficient between each group was 0.587 for single measures and 0.919 for average measures (P=0,001). The concordance between both scores measured by the experts was 0.772 for single measures and 0.872 for average measures (p = 0.001), with similar results when the comparison was made by the students.
Conclusions: The described learning method capacitates a group of students for application and validation of an histological score in a low time-consuming process with the sole equipment of a computer and no need of physical presence.

Key words: Remote learning, medical education

Introduction

The COVID-19 pandemic has limited face-to-face learning and investigation. Under this circumstances medical students have been precluded from presential lectures and hospital practices in many countries. This limits considerably the progress in academic education, forcing professors to adapt to distance teaching. The fact that medical practice learning has classically been in-person has led to a lack of valid distance methods for anatomy or pathology instruction. The current situation demands a rapid but effective adaptation to remote teaching tools.
On other side, investigation has also been impaired by pandemic. Concretely basic researching groups have reduced their activity. These groups are usually multidisciplinary and complex clusters of professionals that need physical gathering. consistent results. The scores may be the most objective and reproducible method to measure histological features such as organic damage. However, pathological analysis implies the availability of a pathologist, increasing the above-mentioned complexity of the organization. We see in the students an available and promising source of researchers who can improve the hypothetical strength of these groups by analyzing histological specimens.

In this respect, a distance learning method for training in pathology scores is needed. Several teaching methods have been described in the literature and no one has concluded to be the best.

Among them, self-regulated learning (SRL) is considered as one of the most valued in lifelong medical education, where acquisition process is self-

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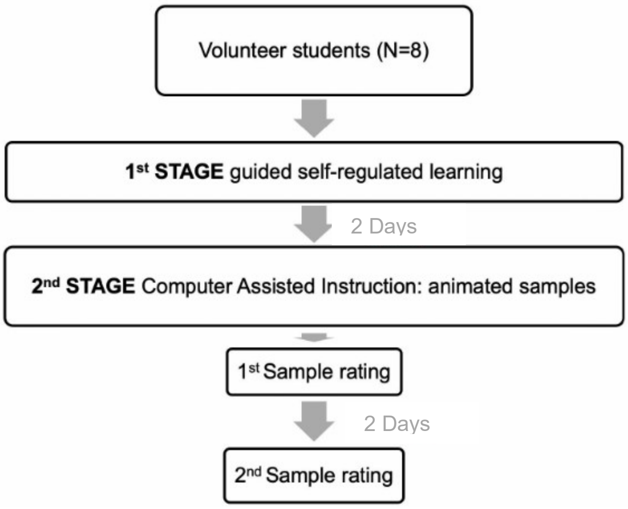

Figure 1. Learning method diagram.

evaluated, self-motivated and self-oriented, generating long lasting theorical concepts(1,2).

As a complement in modern education, computer assisted instruction (CAI) is another useful tool for implementation of specific lessons, which enriches the process of learning and lowers its costs. Regarding to histological sampling, numerous scoring systems have been described for damage assessment. In particular, for ischemic liver damage scoring we account just two of them(3,4). A new score system which mixes some features of the last mentioned may increase the accuracy of damage understanding.

The main research question is whether a structural, remote and low time-consuming learning system is able to capacitate students for the application of an specific scoring technique. The second question is whether a proposed scale for liver injury assessment could be validated in the same way for both trained students and pathology experts. This article specifically addresses the development of a distance, reliable, reproducible, and easily applicable learning system for the utilization of histological scores to hepatic ischemic damage assessment.

Methods

Observers and investigation

Eight volunteer medical students from the University with no previous training in hepatic histopathology were recruited for the study by oral interview. Every student had passed the third year of Medicine. The verbal informed consent was obtained from the participants before initiating the study. The Ethical Committee of Investigation of the Hospital approved this study and it was performed in accordance with the ethical standards in the 1964 Declaration of Helsinki.

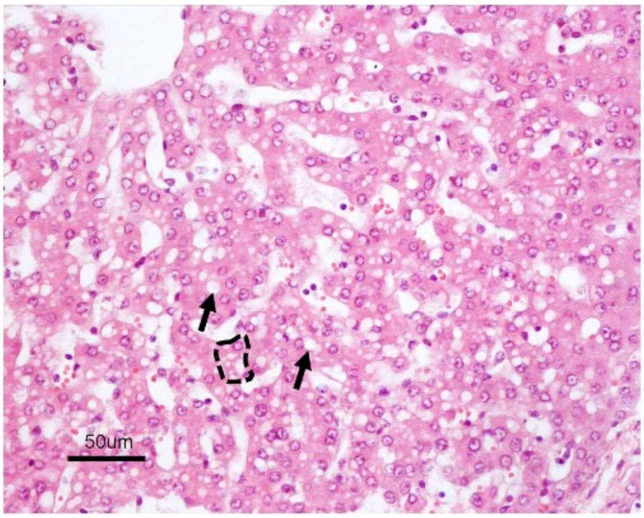

Figure 2. Histological sample hematoxylin/eosin stained at 20x magnification that is used to exemplify liver vacuolization with linear animations.

They were subjected to the learning method that is described below. After this process, liver tissue samples with different degrees of ischemic damage were examined by the students and two professional observers, trained in pathology. A proposed hepatic damage score and the Suzuki score, which served as a standard for validation, were used to rate every piece. Throughout the study a double blind was established, where observers did not know which group the sample they were qualifying belonged to.

Learning method

Based on the hypothesis that a combined intervention can potentiate motivation among learning, we proposed a training process consisting of two stages: a first stage of streaming guided SRL(2,5) and a second stage CAI using animated samples(6).

Since during rest periods, our brain strengthens memories through consolidation, potentially leading to performance improvements, we established a two-day rest period between every phase (**Figure** 1)

At the first stage, teaching was focused on histological and pathophysiological aspects. The different items of the proposed and standard scales were introduced at this point. In this way, the fundamental aspects to be assessed in the histological liver samples and how the observers should assess each item were provided in a written protocol. In addition, complementary image samples and bibliographic sources were provided to complement the self-regulated learning. In this process every student had to plan their own study, set goals, organize, and self-evaluate during the process of acquisition.

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Congestion
1. None
2. Minimun (<10%)
3. Low (10-25%)
4. Medium (25-50%)
5. Severe (>50%)
Vacuolization
1. None
2. Minimun (<10%)
3. Low (10-25%)
4. Medium (25-50%)
5. Severe (>50%)
Sinusoidal Dilatation
1. No
2. Yes
Endothelial Damage
1. No
2. Yes
Bleeding
1. Not present
2. Low (<25%)
3. Medium (25-50%)
4. Severe (>50%)
Edema
1. Not present
2. Periportal
3. Periportal
4. Panacinar
Inflamatory infiltration
1. Not present
2. Low (some portal zones)
3. Low/Medium (most of portal zones)
4. Medium (Confluent <50% of septum)
5. Severe (Confluent >50% septum)
Necrosis apoptosis
1. None
2. Focal (some zone 3)
3. <30% (many Zones 3)
4. 30-60% (Confluent)
5. 60% (Panacinar)

Table 1. Proposed liver ischemic damage score: Items.

In the second stage, practice study was carried out at the histological level, where emphasis was placed on normal and pathological aspects, as well as a structural analysis at the cellular and tissue organizational level. In this way, a streaming training session was carried out via internet in a CAI, where the concepts to be identified were reinforced. Specific training on identifying the normal appearance of the healthy liver and artifacts of histological processing were examined, to later exemplify each of the items (in different degrees of intensity) with various samples. An animation-based learning was used for interactive instruction of each sample, identifying specific cells and basic histological structures (**Figure 2**). During this session, the self-acquired concepts

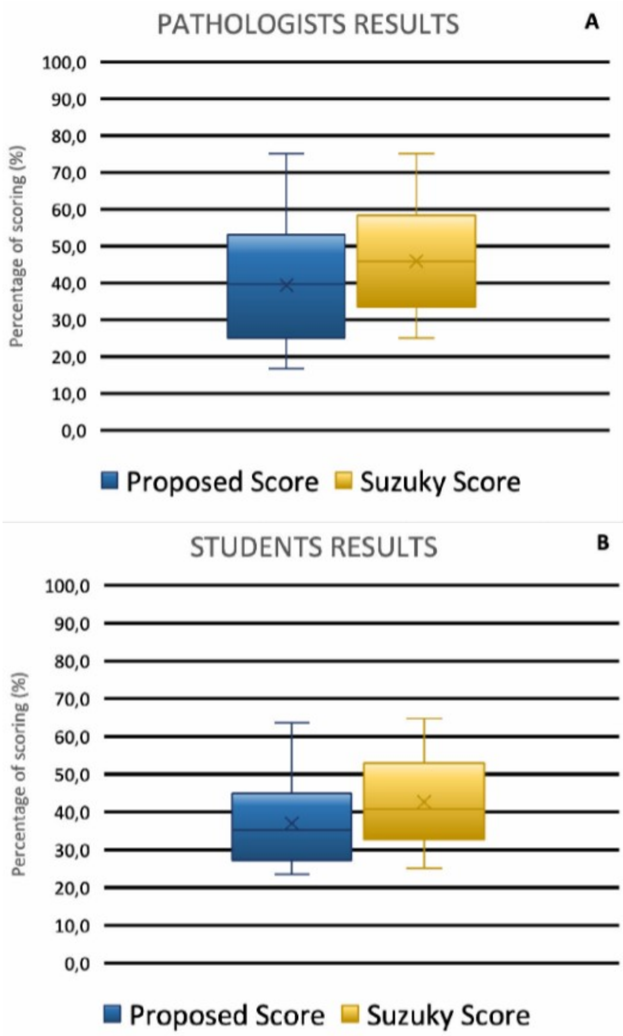

Figure 3. Percentage values of Suzuki Score compared to the proposed Score in experts (N=2) (a) and students groups (N=8) (b) (Madrid, Spain, 2020).

were checked by the teachers in order to avoid misguidance.

With this information, the volunteers carried out a first analysis of the pathological pieces, providing a first rating to each sample that would be reviewed after a second assessment two days after the first. At the end, each observer (students and experts) rated each preparation for both the proposed scale and the Suzuki scale.

Scoring Development and Histological Sampling

An eight items histological score was proposed for hepatic ischemic damage assessment. Two of them were qualitative items whereas the rest were semi-quantitative, as shown in **Table 1**.

For histological sampling, eight porcine livers were subjected to different times of warm ischemia from 0 to 90 minutes using an ex-vivo perfusion machine (7), resulting in a wide range of tissue damage samples.

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Liver biopsies were processed by paraffin embedding and hematoxylin-eosin staining. In order to standardize the areas of analysis, a blinded photograph selection of the samples were examined by the observers. Each observer evaluated each piece at capsular and parenchymal level, at x10, x20 and x40 magnification, assessing portal triad and hepatic lobule structures. In x20 augmentation samples congestion, vacuolation, necrosis/apoptosis, percentage of bleeding, inflammatory infiltration, vacuolation, and degree of edema were assessed. The x40 magnification images were used for characterization of endothelial damage and sinusoidal dilation. The final value of each item corresponded to the highest value within the same histological sample.

Statistical Analysis

The intraclass correlation coefficient (ICC) was used to assess the intragroup agreement at sample scoring between the students and the experienced observers.

For the score validation ICC was employed. The results of the proposed scale obtained by the pathology experts were compared to the Suzuki score (3). After validation, the same comparison was made by the students. An alpha significance level of 0.01 was established.

Results

Eight volunteer students (N=2 males, N=6 females; at fourth medical year) were recruited to carry out the hepatic histological formation and analysis process, which lasted a total of 7 days.

The evaluation of 32 liver samples by the students and the pathology experts was carried out, following the proposed learning and analyzing method. Sample scoring was slightly higher in the expert observers (median = 9,5) compared to the trained observers (median = 8,5) with no significant difference.

The ICC between observers was 0.587 for single measures and 0.919 for average measures, with statistical significance p = 0.001.

For score validation, the two pathology experts rated every specimen with both scales. The median values were similar, where the samples showed 5,5 out of 12 points on the Suzuki scale (46% of the score) and 9,5 out of 24 points on the proposed scale (40% of the score). The ICC showed a concordance between both scales of 0.772 for single measures and 0.872 for average measures, with a statistical significance of p = 0.001.

The same validation was performed by the trained observers. The results were almost the same to the ones obtained by the experts: 5 out of 12 on the Suzuki scale (42%) and 8,5 out of 24 points on the proposed scale (35%) (ICC: 0.796 for single measures; 0.886 for average measures, p = 0.002). **(Figure 3)**

Discussion

The main research question may be answered as partially affirmative, as the described learning method capacitate the group of unexperienced observers for application of a specific scoring technique in just 7 days with no need of physical gathering. As shown by the results, the main disadvantage of the method is that the accuracy of the observers is optimum when average values are taken, but it is not acceptable when single observer's is taken. This method capacitates more the group rather than the individual. On the other hand, the second question should be answered affirmative. The validation of the proposed score shown similar correlation rates between the pathology experts and the trained students, suggesting that the teaching method enables the scholars for specific score validation.

Learning method

In medical education, many approaches have been described for appropriate skill acquisition, but no one have demonstrated to be the best. From our knowledge, there is no single perfect method for pathology learning. As this acquisition process is multifactorial, we suggested a mix of different learning techniques which combined CAI and SRL.

Self-Regulated Learning

All students are responsive to some degree during instruction; however, students who display initiative, intrinsic motivation and personal responsibility achieve particular academic success (8). These are considered to be self-regulated learners. They carry responsiveness to feedback their learning, and self-perceptions of their academic accomplishment, undertaking self-monitoring and self-assessment at different stages during the learning process. Since SRL, considered to be a great tool for practice acquisition, helps students to accept greater responsibility for their own learning in the present and to become lifelong learners (5,9), we proposed an initial approach of SRL for academic instruction during the learning process.

SRL theories of academic achievement are distinctive from other accounts of instruction by their emphasis on how students select, organize, or create advantageous learning environments for themselves

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and on how they plan and control the form and amount of their own instruction.

Consequently, self-regulated learners are actively involved in learning processes by using three components (metacognitive, motivational, and behavioral) to achieve their academic goals. Teachers should control and boost these components to improve SRL process by using specific strategies (2,8). The SRL strategies are actions directed at acquiring information or skills by learners, increasing their self-efficacy. These procedures increase self-motivation resulting in a positive feedback, improving the SRL development. In this way, motivation is not just a result but a necessary part of the method, which initiates the learning progression. Thus, learning strategies cannot be implemented effectively without the essential motivation (10). In our research, we proposed to motivate the observers making them part of the investigation and encouraging them to become transcendental in science progress.

During SRL process, two aspects should be taken into account avoiding misleading of guidance process (5,11). The proposed activity should not be conducted entirely within the learner with little or nonexistent support of the teacher; and the design of a SRL activity is not sufficient to promote both learning and the development of self-regulation, because motivation is a necessary part of the equation as said before. Therefore, medical educators must assume responsibility for designing environments that afford the opportunity for self-regulation and providing support for the self-regulating processes. In our method we instructed the students in self-regulated aspects, motivated them during experimental development, and checked and supported their learning process by oral interviewing in the second stage. Once initiated the SRL it was maintained during the whole learning method, potentiating the following procedures.

Computer Assisted Instruction

Literature reviews of evaluation studies show that CAI is an effective and time-efficient learning method in a wide range of contexts, improving medical education (6,12,13). The main advantages of CAI consists on no need of physical attendance, flexibility, time-efficiency, low cost, and interactivity which enhances independent learning and problem solving.

Modern CAI programs have become dynamic tools in which the learner plays an active role. Due to the use of multimedia (text, pictures, sound and video) CAI applications can be presented in a lively and attractive way, which suits to anatomical and histological learning.

The main problem at teaching pathology with image samples is that, generally, people understand pictures, including photographs and video recordings, as impartial representations of something that exists in the natural environment(14), which can mislead concepts. In this respect, animation can help students overcome the visuospatial and temporal barriers inherent in static depictions. However, we must take this tool carefully, since improperly constructed animations could also generate ambiguities into a student’s mental model (15).

The use of this animations has been described as part of interactive multimedia programs to replace the traditional lecture/laboratory-based histology course. In these programs, linear and non-linear animations have been used for proper pathology learning improving the development of mental models (13). In the present article, histological samples were mixed with interactive animations in a CAI model, for score practice learning. As showed by the quick concept acquisition process, we believe that this hybrid method helped the student to develop better mental models, and it was enhanced by the previous initiated SRL.

Scoring Validation

Histopathologic scoring is a tool by which semiquantitative data can be obtained from tissues. Using a validated scoring system improves reliability of observations and comparability of these observations with results from other research groups. It is therefore important to know not only if a score has been validated, but also how the ‘validation’ was performed. Validation of a score may occur through comparison to already validated macroscopic scoring systems, to other already validated histological systems, to automated (and validated) histomorphometric systems or to biochemical parameters(16). In the present article, we compared a new score with a previous validated score.

Concerning to the specific case of liver ischemia-reperfusion damage, one of the most used scores is the already mention Suzuki’s score(3), which includes venous congestion, vacuolation and necrosis from 0 to 4 (17,18). In other experimental studies, they use a generic score that encompasses several aspects to give a generic idea of the presence of damage such as nuclear and cytoplasmic changes (pyknosis, vacuolization, hypereosinophilia), hemorrhage, and inflammatory infiltration (19). One important aspect to remark is the degree of neutrophilic infiltration in the lobes and in the perivenular region, since ischemic damage triggers this inflammatory response (4). In every score, when different degrees of the same item are present in the biopsy, the highest degree is assigned.

An important issue to take into account in the validation process is the blindness. Masking of the pathologist to experimental groups is often necessary to constrain bias, and multiple mechanisms are available, the one used in our experiment is the blinding of the samples for the observers.

Regarding the before mentioned aspects, our research group designed the proposed score that unifies the features described, including endothelial damage which is caused by hemodynamical and inflammatory alteration in ischemic process (as shown in Table 1). The results obtained in our study supported the proposed score and suggested that the teaching method is useful for training observers in validating histological scales.

Limitations of the Study

The main limitation of this study is [illegible] number of participants and the need of a group of observers to evaluate the samples since single measures are not accurate. [illegible] would be interesting to extrapolate this step learning method to other pathological scores in various experimental groups to reinforce its real potential.

Conclusion

The use of the described step learning method that enhances CAI animated models with SRL capacitate a group of unexperienced observers to apply histological scores in the COVID-19 era with a fast and low-cost procedure, potentiating investigational groups with no need of physical presence.

This method enables the student to apply and validate liver histological scores and be able to participate as part of experimental researches. This teaching scheme should be contrasted with another pathological scores in further studies.

Conflicts of interests

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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