http://dx.doi.org/10.1590/2317-6431-2016-1782

The purpose of this letter is to present some insight of my experience in performing a diagnostic clinical trial in dysphagia. The goal of the diagnostic clinical trial is to determine if a new test works and if it is safe. The validation of a diagnostic test is a process of growing complexity. This process is divided in two steps: validation of the performance of the new test and validation of this test as a diagnostic clinical trial. Our diagnostic trial was based on a research protocol called DREP (Dysphagia Risk Evaluation Protocol). This protocol is being tested since 2007. During these 10 years our protocol was used and analyzed, with a strict methodology, in approximately 500 individuals. These studies involved master thesis and doctoral dissertations that explored the variabilities of the test. The DREP is routinely used in patients at the *Hospital das Clínicas* of the School of Medicine of the University of São Paulo (HCFMUSP) and is constantly discussed in our clinical and multi-professional meetings. The DREP has been used in more than 6,000 patients over the last 9 years.

The DREP is being validated according to the different phases proposed for diagnostic clinical trials, as follows:

- DREP – Diagnostic trial Phase I: the purpose was to evaluate the safety and to identify possible undesirable effects of the test. This phase, which started in 2006, involved the construction of the DREP. The protocol was constructed with the purpose of aiding speech-language pathologist to identify and interpret alterations in the swallowing dynamics, to characterize clinical signs that suggest possible laryngeal penetration or aspiration, to define the severity of dysphagia and to stablish an appropriate approach based on the results of the assessment. The DREP was elaborated based on existing protocols at the time. Common points were identified, none common points were excluded and the items judged as relevant were included. The DREP has three parts: a water swallow test, a swallow test with pasty foods, the classification of dysphagia severity and possible therapeutic approaches. The protocol was submitted to the assessment of judges (3 speech-language pathologist who had experience in the field) and obtained a high level of agreement (i.e. above 75%). At that moment, 10 years ago, the construction of the test aimed to give speech-language pathologist the most complete instrument possible to determine, still at the bedside, the risk of dysphagia. This action was necessary to attend the norms of HCFMUSP, where standardized operational procedures are required from all areas. At that moment we did not perform the internal validation of the protocol since we considered that the DREP was too long to contemplate all of the risk aspects involved in swallowing disorder (i.e. dysphagia), and it would make no sense to reduce the items without verifying population performance. Two studies were published during this phase[1,2].

- DREP – Diagnostic trial Phase II: the purpose was the application of the DREP in different risk populations (head trauma, stroke, prolonged orotracheal intubation) and in patients with different overall health status (emergency, intensive care unit, infirmary) to evaluate its efficacy and safety. In this phase approximately 500 patients were tested. The first internal

validation of the test was performed considering the total number of tested patients. The items identified as predictors of the risk for pulmonary penetration/aspiration were: presence of multiple swallows; altered cervical auscultation; altered vocal quality after swallow and presence of cough and/or choking after swallow. Also in this phase we performed a study to correlate the items of the DREP with the overall health status of critical patients. The results of this research indicated that patients with ages above 55 years, time of prolonged orotracheal intubation >6 days, score ≥5 points on the SOFA (Sequential Organ Failure Assessment), score ≤14 points on the Glasgow Coma Scale and who presented, according to the DREP, altered cervical auscultation and cough/choke were considered high risk for pulmonary penetration/aspiration and should be immediately referred to an objective assessment[3,4,5,6,7,8].

- DREP – Diagnostic trial Phase III: this is the phase of validation where we find ourselves now. This phase is already underway and the purpose will be to use the DREP in different risk population (head trauma, stroke, prolonged orotracheal intubation) and to compare these results to the results of the videofluoroscopy of swallowing (VFS) (i.e gold standard). The validation of the DREP will only be concluded when its results, in comparison to the gold standard (i.e VFS), indicates that the protocol is capable of indicating who is truly at risk for presenting pulmonary penetration/aspiration. In this phase, the analyses of the DREP will involve:

1. Sensitivity: indicating if the DREP is sensitive in identifying the person who really presents the risk for pulmonary penetration/aspiration;
2. Specificity: indicating if the DREP is specific in identifying the person who is not at risk for pulmonary penetration/aspiration;
3. Positive predictive value: indicating the proportion of people who are truly positive considering those who were identified as positive by the DREP;
4. Negative predictive value: indicating the proportion of people who are truly negative considering those who were identified as negative by the DREP;
5. ROC curve (Receiver Operator Characteristics): the ROC curve will determine the cut off points based on the results of sensitivity and specificity.

- DREP – Diagnostic trial Phase IV: after the validation of the DREP in phase III, its final version will be used safely in different populations and the results will be compared among different reference centers.

Nowadays the Division of Oral Motor Disorders is responsible for 4% of all procedures performed at the Central Institute of HCFMUSP, the largest school hospital in Latin America. Most of the procedures performed by our team are related to patients with dysphagia.

A good clinical protocol should be in constant development. Even in the presence of new diagnostic technology, a clinical protocol is indispensable, especially when considering that technology is not always available to all patients and professionals. New technology usually

comes at high costs (not only when considering the equipment itself, but also for the required professional specialization) and can, in some cases, involve invasive procedures. Ideally, the end point of this process is to have a validated clinical protocol, which effectively attends the needs of each Institution.

Claudia Regina Furquim de Andrade
Department of Physiotherapy, Speech-Language and Hearing Science and Occupational Therapy, School of Medicine, Universidade de São Paulo – USP – São Paulo (SP), Brazil

REFERENCES

1. Padovani AR, Moraes DP, Mangilli LD, Andrade CRF. Protocolo fonoaudiológico de avaliação do risco da disfagia (PARD). Rev Soc Bras Fonoaudiol. 2007;12(3):199-205. http://dx.doi.org/10.1590/S1516-80342007000300007
2. Padovani AR, Moraes DP, Sassi FC, Andrade CRF. Avaliação clínica da deglutição em unidade de terapia intensiva. CoDAS. 2013;25(1):1-7. http://dx.doi.org/10.1590/S2317-17822013000100002
3. Moraes DP. Indicadores de prognóstico clínico da deglutição funcional em pacientes de um hospital público de grande porte [tese]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2012.
4. Medeiros GC. Disfagia orofaríngea em pacientes submetidos à intubação orotraqueal prolongada em UTIs [dissertação]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2012.
5. Moraes DP, Sassi FC, Mangilli LD, Zilberstein B, Andrade CRF. Clinical prognostic indicators of dysphagia following prolonged orotracheal intubation in ICU patients. Crit Care. 2013;17(5):R243. http://dx.doi.org/10.1186/cc13069
6. Medeiros GC, Sassi FC, Mangilli LD, Zilberstein B, Andrade CRF. Clinical dysphagia risk predictors after prolonged orotracheal intubation. Clinics. 2014;69(1):8-14. http://dx.doi.org/10.6061/clinics/2014(01)02
7. Medeiros GC. Preditores clínicos do risco de disfagia pós intubação orotraqueal prolongada [tese]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2015.
8. Medeiros GC, Sassi FC, Zambom LS, Andrade CRF. Correlation between the severity of critically ill patients and clinical predictors of bronchial aspiration. J Bras Pneumol. 2016;42(2):114-20. http://dx.doi.org/10.1590/S1806-37562015000000192