

Review

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of
the Dissertation by Dr. RadinTsonev Tsonev
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for the the educational and scientific degree “Doctor” in Internal medicine

Titled ”Evaluation of liver fibrosis using transient elastography – Fibroscan and the quality of life in patients with chronic hepatitis C and liver cirrhosis”

Scientific supervisor: Prof. Dr. S. Stoynov PhD

The submitted for review dissertation titled ”Evaluation of liver fibrosis using transient elastography – Fibroscan and the quality of life in patients with chronic hepatitis C and liver cirrhosis” by Dr. RadinTsonev Tsonev is well structured. It's 109 pages long, includes 48 tables, 13 figures and 8 graphics.

The postgraduate doctorate student has followed the results and studies of 125 authors, 6 of which Bulgarian, most of them written after 2000, and 35 after 2010, thus making the thesis relevant to modern medicine. All of the results used in the thesis are acquired at the Clinic of Gastroenterology Acibadem City clinic Tokuda Hospital Sofia.

The incredible results in the treatment of chronic hepatitis B and C has imposed on researchers to systemize and synchronize the methods for evaluation of liver fibrosis to juxtaposition the data from different countries and teams and propose the optimal treatment protocols as well as patient follow up in the future.

This is particularly important considering previous experience with treating HBV that liver fibrosis is reversible, especially if treatment begins in the early stages of infection. The dramatic changes in HCV treatment has made liver fibrosis evaluation very important. The first steps when using new medications are made with not severely ill patients. It is hard to find drugs that are effective and safe in advanced liver disease. The increasing usage of DAAs requires easily performed methods for evaluation of liver fibrosis.

On the other hand it is known that the life expectancy of patients is reduced in disease progression and end stage liver disease, as well as patients' anxiety associated with having a chronic illness. The methods for evaluating the quality of life are hard, not easily comparable and are ethnicity specific. It is accepted that the quality of life is an integral indicator of the condition, achievements and success of the individual, their family, society as well as the status of government. The self evaluation of a patient's quality of life and their health status is important in motivating them to continue therapy.

It is clear that chronic hepatitis C can be easily eradicated with even shorter treatment regimens– 2 months currently. There are still questions such as should there be treatment after SVR, how to assess the illness, how it changes the patients' lives. Some of these answers can be found in Dr Tsonev's dissertation.

Only one objective is proposed in the thesis. In fact there are two. It is of great significance - comparison between measuring liver fibrosis using transient elastography – Fibroscan and liver biopsy in patients with chronic hepatitis C and liver cirrhosis, because these findings can affect the health politics in Bulgaria regarding chronic hepatitis. Furthermore, there is the secondary nuance of the thesis – measuring the quality of life of people with chronic liver disease.

Six tasks have been formulated - comparing histology and blood work with results from TE-fibroscan in patients with different stages of liver fibrosis, fibrosis dynamics, quality of life, disease control.

The results from 366 patients have been analyzed during an interval of 2 years, equally divided by sex – 240 patients with HCV, 37 cirrhotic patients, 88 patients with HBV. In a subgroup of 149 liver fibrosis was measured using TE-fibroscan before and 12 months after therapy with DAAs.

A specific questionnaire was used in the survey for assessing the quality of life (SF-Health survey) SF-8, scientifically valid and reliable for the physical and psychological status.

The statistical analysis is diverse – descriptive statistics, correlation analysis, regressive analysis, dispersion analysis, discriminant analysis.

The results are well detailed and mathematically solid. Special attention was given to comparing results from TE-fibroscan and liver histology in different diagnosis.

In lower level of fibrosis there was correlation in 30% and non correlation in 70%. In intermediate fibrosis the correlation was 56,75% and non correlation 43,24%, in advanced fibrosis the correlation was 79,2% and non correlation 21%. This made necessary using another non invasive marker – Fibrotest or APRI. There is a linear correlation between histological activity score and TE-Fibroscan results – the more advanced fibrosis, the higher the comparability of the methods.

The results are in concurrence with the international results and guidelines of not requiring liver biopsy when assessing liver fibrosis in chronic HCV and HCV-cirrhosis. It is however recommended to use another noninvasive methods together with TE-fibroscan. Whether it is cheap one such as APRI/FIB-4, or more expensive like Fibrotest/FibroMAX is up to the physician.

Dr Tsonev is comparing the most commonly used (even in clinical trials) elastographic methods with liver biopsy in a significant amount of patients, thus giving us the opportunity to look at the results from a different perspective, not to be falsely guided by the measurements, not to reject clinical judgement and to recommend a biopsy when necessary. It is clear that the long term consequences of chronic disease after SVR are yet unknown.

The incredible success in treating chronic hepatitis C changes the psychology of the patients and gives them hope.

The literature review is quite extensive. The problems of fibrogenesis are examined, which is not the subjective of the thesis.

Seven conclusions have been drawn out, which are well formulated and correspond to the full extent of the study results – assessing liver fibrosis using noninvasive methods, which are precise, have a low cost, are easily performed and have a great impact on treatment and disease regression. Liver biopsy cannot be used for screening. For optimizing noninvasive methods, combined algorithms are recommended. Improving quality of life should also be a treatment objective.

I accept the six contributions – most significantly liver fibrosis cutoffs in HCV and improving the quality of life.

Dr Tsonev is introducing publications on the matter dating back to 1996 both in Bulgarian and English.

In conclusion, Dr Tsonev is a well-established clinical physician and gastroenterologist with a long academic experience.

Dr Radin Tsonev Tsonev has developed a scientific dissertation in concurrence with the Law and regulations for granting the educational and scientific degree “Doctor” in the clinical specialty “Internal medicine”.

In this regard I recommend to the panel to vote positively for Dr Tsonev.