

Statement

by prof. Dr Krasimir Antonov Antonov
Clinic of Gastroenterology
St. Ivan Rilski Hospital Sofia
Department of Internal Medicine, MF, Medical University Sofia

on the Dissertation for the Educational and Scientific Degree “Doctor” by Dr. Radin Tsonev Tsonev Doctoral student in self-study, 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 dissertation by Dr. Radin Tsonev is on a relevant topic in modern hepatology, specifically comparison between histological assessment of different stages of liver fibrosis in chronic hepatitis C and various noninvasive methods; as well as the effect of disease before and after eradication of chronic HCV using DAAs on the quality of life of patients.

The thesis is well structured and according to requirements – introduction, literature review, objectives, tasks, materials and methods, results and discussion, main conclusions, bibliography. It is written in clear scientific Bulgarian and is 111 pages long.

The abstract is 54 pages long (49% of the thesis) and it well reviews the main sections of the thesis.

The introduction is 4 pages and contains the main points of the literature review.

The literature review taking 42 pages (38% of the dissertation) is relevant. It studies the social significance and epidemiology of chronic HCV, the role of liver biopsy in the diagnostic process, noninvasive methods for measuring liver fibrosis, quality of life and quality of healthcare in the context of diagnosis and treatment. The small number of Bulgarian authors on the subject must be noted.

The bibliography contains 125 sources, only 18 of which (14,6%) are published in the last 5 years. This seems a little odd considering the number of foreign publications on the matter.

The objective of the dissertation is clear - comparison between measuring liver fibrosis using transient elastography – Fibroscan and liver biopsy in patients with chronic hepatitis C and liver cirrhosis, and the effects of treatment, as well as the quality of life of patients with chronic liver disease.

The six tasks are well defined to support the main objective.

The study groups and the utilized methods are written on 11 pages. For the period 2016-2018, 366 patients with chronic HCV and cirrhosis were studied, between ages 18-75, 193 males and 173 females. From them 241 were with chronic HCV, 37 with cirrhosis, 88 with chronic HBV. In all the patients TE-fibroscan was performed with results in kPa, stages of fibrosis from 1 to 4, blood levels of ASAT and ALAT were measured. Liver biopsy was performed using the Menghini method or True-cut with more than 8 portal spaces, the severity of histological changes was made using the Metavir scoring, specific questionnaire was used for assessing the quality of life (SF-Health survey) SF-8, scientifically valid and reliable for the physical and psychological status.

In a subgroup of 159 patients liver fibrosis was measured using TE-fibroscan before and 12 months after therapy with DAAs. The device Fibroscan (Echosens) measures the speed of sound waves going through the liver and then transforming it into liver stiffness in kilopascals.

For the statistical analysis the software product Module SPSS Statistics Base 23 from IBM Statistics was used. The results of each patient were processed using descriptive statistics, correlation analysis, regressive analysis, dispersion analysis, discriminant analysis.

Significant results were produced, described on 33 pages. Most importantly:

there is a correlation between liver fibrosis measured using TE-Fibroscan and results from liver biopsies. This correlation is most evident in patients with advanced fibrosis F3 and F4, and less in lower stages of fibrosis F2 and F1. There is no connection found between fibrosis and

cytolytic activity – ASAT, ALAT. The measurements of liver fibrosis made using the TE-Fibroscan before and after treatment show a statistically significant difference.

Age differences are not a factor impacting the self estimation of the quality of life. The survey shows a connection between the questions, and the question about the psychological experiences during illness is with the lowest correlation with the other questions. The psychological state and emotions regarding disease, treatment and recovery are major factors when estimating the quality of life. These experiences are not age specific, thus showing that social experience does not affect the quality of life.

The discussion and conclusion take 5 pages. They summarize the results and their relevance to modern knowledge.

Seven conclusions were made that correspond well with the results. There are 6 contributions.

I accept the stated conclusions and contributions, with the exception of those regarding the change in liver fibrosis evaluated with TE-Fibroscan after successful eradication of chronic HCV, because there was no histological verification of the specified changes in the current dissertation. Very important for the clinical practice are the factors that impact the quality of life, as well as the proposition to form a multidisciplinary team to help with the treatment and recovery process.

The results in Dr Tsonev's dissertation have a scientific and practical significance and lead to expanding our knowledge in the diagnosis and monitoring of liver disease in patients with chronic HCV, and show the major factors concerning the quality of life in patients treated with DAAs.

In conclusion, based on the aforesaid, Dr Tsonev's dissertation is complete with clear objectives and tasks, original results, defined conclusions and important contributions. It is developed in concurrence with the Law regarding the development of scientific cadres and regulations for acquiring a scientific degree in Acibadem City Clinic Tokuda hospital Sofia.

I recommend to the panel to grant Dr Tsonev the educational and scientific degree “Doctor”.

19.09.2019

Prof. K. Antonov