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Opponent's review: doctoral dissertation

Shiann-Guey Yang, MD

Selected differences in patophysiology of cardiovascular system in women

Submited work itself has 121 pages, 11 pages of abstracts/content, 23 pages of references (majority of them published in last years/decades) a 4 in extenso articles with impact factor. These articles supports application of work. Primarily the number of articles is higher than necessary (it is doubled). Secondarily the first abstract was published in 2010 which confirms systematical scientific activities of Dr. Yang under supervision and in cooperation with Prof. O. Kittnar, Head of Institute of Physiology and coworkers. While executing the experiments Dr. Yang used the well equiped Center of human physiology and pathophysiology in Institute of Physiology in Albertov.

The choice of topic is up-to-date also from the clinical point of view – differences between men and women in patophysiology, clinical circumstances and outcome have been studied in the past years frequently. Results of these studies impacts treatment of cardiovascular diseases. Resuts of some clinical trials with hormonal substitution as therapy casted doubt on hypothesis, that the dramatical rise of incidence of coronary heart disease in postmenopausal women is caused by loss of protective effect of circulating estrogens.

Summary of dissertation corresponds to the usual division into parts: „Introduction", „Hypothesis", „Methods", „Results" and „Discussion" and dissertation itself is divided in chapters. Chapter 1 is mostly composed of theoretical background, Chapter 2 describes methods and results of two most important studies, results are discussed.

In the beginning of theoretical background the role of sex-hormones influence on cardiovascular system is mentioned. Next part describes application of cardiac monophasic action potencial. Then sex-difference in ten important types of arytmias is analysed. This part is complex, profound in thought and logically structured.

The following chapters analysed phenomenon of sex-difference in cardiovascular disease, besides the above mentioned effect of circulating estrogen is also the description of difference of

mechanism in myocardial ischemia-reperfusion injury. At the end of chapter patophysiological and clinical aspects of pregnancy and postmenopause are discussed.

Study 1 investigated gender differences in patients with ventricular tachycardia with origin in right ventricular outflow tract treated by radiofrequency ablation. According to this study women have a shorter QRS interval and lower ventricular voltage. Differences in short and middle-term outcome were not found inbetween sexes.

In Study 2 influence of different types of hormonal substitution therapy on heart rate variability was studied. Significant difference was found only in women treated by estrogen alone, results in women with combined hormonal substitution therapy are similar to untreated women. This study involved impressive number more than 900 volunteers from Taiwan devided in 5 groups. Despite of this autor very critically presents limitation of study.

The work is fully acceptable in terms of formal structures.

I have two question for Dr. Yang:

- what about right ventricular systolic function measurement, why was the parameter of ejection fraction (in Study 1) used?
- are there sex differences in atrial flutter patients too?, are they similar to atrial fibrilation?

The work is based on correct patophysiological concept, is appropriately done and with possible impact for clinical implementation and future research. **Shiann-Guey Yang M.D. fulfils** in my opinion all that is necessary to receive a title od **Ph.D**. and I **recommend** it.

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