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# **HEART AND LUNG FUNCTION- IN HEALTH AND DISEASE**

## **Methodological studies in Clinical physiology**

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### **Akademisk avhandling**

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Bergasalen, Norrlands Universitetssjukhus, fredagen den 1 december, kl. 13:00

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**Abstract**

**Background:** The human heart and lungs constitute an intricate and dynamic system. Various clinical physiological examinations can be used to evaluate cardio-pulmonary function and identify abnormalities. To distinguish normal from abnormal findings in a patient population compared to healthy controls, adequate, accurate and up-to-date reference materials are required. There is currently a lack of well-established sex and age specific reference materials that clearly state boundaries of normality for electrocardiography (ECG) variables. For lung function examinations there are several different reference materials available. In addition, the relation between lung function, age, sex, and height has generally been difficult to model in an optimal way. Heart rate variability (HRV) is a method for evaluating the autonomic nervous system (ANS) and its influence on heart rate and blood pressure. It is well known that decreased HRV is associated with increased mortality. Autonomic imbalances are also associated with various pathological conditions, of which rheumatoid arthritis (RA) and ischemic heart disease (IHD) are studied in this thesis.

**Aim:** To describe the properties of different clinical physiological examinations to assess the cardiovascular and pulmonary systems in healthy individuals regarding age and sex. In addition, to assess the relationship between HRV, RA and IHD both cross sectionally and longitudinally.

**Results:** Sex- and age dependent differences were found in ECG examinations in the studied population (n=219). This emphasizes former findings and supports the need for the establishment of age- and sex - specific reference values in the future. Lung function examination in subjectively healthy subjects (n=285) support and emphasize that the reference values presented by Global Lung function Initiative (GLI) underestimate the pulmonary function in the adult Swedish population. The study showed that the model used in GLI can be updated with new values that are specific for the Caucasian population in Sweden. Patients with RA (n=50) presented with lower HRV than controls (n=100) during autonomic provocation tests, both at baseline examinations and after five years. This indicates a cardiac autonomic imbalance. Furthermore, increased systolic blood pressure was associated with reduced HRV, thus a decrease in HRV could be a risk marker for developing arterial hypertension in this patient group. Females with IHD, (n=197) presented with lower HRV compared to controls (n=141) at baseline, and higher mortality rate after 15 years. The higher mortality rate was only present in females < 60 years-of-age. For measurements obtained in the upright position, HRV was higher in females that died during follow-up compared to those who were alive.

**Conclusion:** This thesis emphasizes the importance of validated and updated sex- and age specific reference materials and models that are well suited for different clinical physiological examinations. Additionally, HRV examinations exposed changes in the ANS related to RA as well as IHD, where findings were shown to be persistent over time and particularly pronounced during provocations. In the future, HRV assessment could be a useful tool to identify the increased risk of developing hypertension in patients with RA, or to customize treatment based on ANS response as the field of personalized medicine continues to evolve.

**Keywords**

Clinical physiology, Reference materials, ECG, Dynamic spirometry, HRV, rheumatoid arthritis, cardiovascular disease, ischemic heart disease.

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