The rationale of a longer life span and nuclear medicine

Andreas Otte[1] MD, Konrad Wink[2] MD

1. Biomedical Engineering, Faculty of Electrical Engineering and Information Technology, University of Applied Sciences Offenburg, Badstr. 24, D-77652 Offenburg, Germany, E-mail: andreas.otte@hs-offenburg.de,

2. Medical Faculty, Albert-Ludwigs-University Freiburg

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Abstract

Routine nuclear cardiology examinations indicate heart rate, cardiac rhythm, the height of cardiac pulse and respiration rhythm. It would be of interest to study whether these data, especially if the same tests are repeated, can indicate patients' well being in the future and perhaps patients' life span, other factors being equal. Related old theories and suggestions are mentioned. Furthermore, some drugs like I-f channel antagonists and stress tests testing cardiac reserves could support such a study.

Introduction

The aim to forsee forthcoming diseases and to live longer has been expressed and studied long ago in ancient Egypt, Greece and other countries. In China, e.g., Taoist monks practiced the ritual of self-mumification in the 5th and 6th century a.c. to reach immortality. They controlled physiological functions by meditation and diet. By drinking a kind of glue the monks finally sealed their gastrointestinal tract and died; their corpses were dried and sealed with further external glue.

Indeed, embalming is only one approach of man to achieve eternity. Egyptians mummied the dead in order to live sometime later and Greeks for the same purpose kept them in special rooms with all their belongings. The aim to find out how to live longer has stimulated and is stimulating medical research. There are some epidemiological studies indicating a specific relationship between mean heart rate at rest and mortality in healthy man such as the Framingham Heart Study [1] or the CORDIS study [2]. This relationship could be seen clearer in patients with stable coronary artery disease, hypertension, left-ventricular systolic dysfunction, myocardial infarction and heart failure as in the BEAUTIFUL study [3], the SHIFT study [4-6], the INVEST study [7], or the recent eplerenone study [8].

In the following, we would like to focus on some of these studies in more detail: In the Framigham study [1], at entry into the study, 5070 subjects were free of cardiovascular disease. Followed-up over 30 years, there was a relation of resting heart rate on biennial ECG examinations, to mortality rates. Based on 1876 total deaths and 894 cardiovascular deaths, in both sexes, at all ages, all-cause, cardiovascular, and coronary mortality rates increased progressively in relation to antecedent heart rates determined biennially. There was also a substantial excess of non cardiovascular deaths at high heart rates.

The BEAUTIFUL study [3] is a randomised, double-blind, placebo-controlled trial of 10,917 patients who had coronary artery disease, with left-ventricular ejection fraction of less than 40% and received 5 to 7.5mg Ivabradine twice a day or placebo. Median follow-up was 10 months. Ivabradine reduced heart rate by 6 bpm (SE 0.2) at 12 months, corrected for placebo. In addition to study drugs, 87% of patients were receiving í-blockers. The primary endpoint was a composite of cardiovascular death, admission to hospital for acute myocardial infarction and admission to hospital for new onset or worsening heart failure. Ivabradine did not improve cardiac outcome, but could be used to reduce the incidence for coronary artery disease (CAD) outcomes in a subgroup of patients who had heart rates of 70bpm or greater. Of course CAD is a main factor shortening life span.

In the SHIFT trial [4-6], a randomised, double-blind, placebo-controlled study, 6558 patients with symptomatic heart failure and a left ventricular ejection fraction of 35% or lower, with sinus rhythm and heart rate 70bpm or higher, had been admitted to hospital for heart failure within the previous year, and were on stable background treatment including a í-blocker if tolerated. Patients were titrated to 7.5mg ivabradine twice daily or placebo. The primary composite endpoint of cardiovascular death or hospital admission for worsening heart failure was improved, driven mainly by hospital admissions, but cardiovascular mortality was not reduced significantly.

To determine the relationship between resting heart rate and adverse outcomes in coronary artery disease 22,576 patients, were enrolled in the randomized, reference-controlled INVEST study and treated for hypertension [7]. Different resting heart rate lowering strategies were used (verapamil, atenolol). Higher baseline and follow-up heart rates were associated with increased adverse outcome risk. On treatment resting heart rate was more predictive for adverse outcome than baseline resting heart rate.

Efforts from medicine and possible role of nuclear medicine for longer life span

Although an unhealthy environment capable to develop diseases has been promoted during the Baroque time [9, 10], or earlier, advances in medicine helped to increase life expectancy. Among others, we would like to mention the biomedical engineering developments in radiology and nuclear medicine since the 1960s. In addition to heart motility and ejection fraction, nuclear medicine can also diagnose other parameters that influence life span, such as atherosclerosis etc and relate these parameters if studied in sequence to heart rate, breath rate, body weight and other factors, with the overall survival of the persons studied. Furthermore, nuclear medicine is able

to support basic research on cellular reproduction of the tissues (and its limitations) by labelling DNA and also a number of nutritional factors to study the progress of aging [11].

Can we forsee and increase our life span by studying cardiac or other diagnostic procedures of nuclear medicine and treating them by í-blockers, the I-f channel antagonist ivabradine (Procoralan®), or even by pace makers? [11] The question of whether we have to die earlier, if our heart rate is increased is provocative. It is not easy to determine endpoints with myocardial perfusion studies or to find out the reason of our decadence.

In conclusion, attempts to increase our life span or live another life are old. Medicine and nuclear medicine have long tried to face the dangers of shortening life span. Upon decreasing mean heart rate with cardioactive drugs and measuring various cardiac and respiratory parameters, nuclear medicine can investigate the route to a longer life span. We need more specific clinical studies with large populations, preferably of healthy volunteers, over many years, and this would raise at least ethical issues.

The authors declare that they have no conflicts of interest

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