At the other end of the spectrum, patients with acromegaly, who are suffering from excess secretion of growth hormone, also exhibit elevated mortality rates in cardiovascular and cerebrovascular diseases {12}. Contributing factors to this mortality are found in the higher prevalence of hypertension, diabetes, arrhythmias and cardiomyopathy with hypertrophy of the heart {13}, {14}. Inhibiting the hGH secretion with somatostatin analogs in these patients has shown beneficial effects on heart structure and performance {15}. Further demonstration of the detrimental effects of hGH excess is made by the study by Takala *et al.* in 1999 where administration of high-dose hGH to critically ill patients in a intensive care unit doubled the mortality rates compared to placebo {16}.

Most of the literature concern patients with either excess or deficiency of hGH. However the prospective study of French policemen started in the late 60's and early 70's with an 18 year follow-up, examined fasting values of hGH and the risk of premature mortality. Their findings show that higher levels of hGH after a 2h oral glucose tolerance test are associated with an elevated risk of premature mortality of all causes and of cardiovascular disorders, fasting hGH (measured with standard hGH test was not significant for prediction of mortality {17}. Using a 0.5ng/ml cut off value, Maison *et al.* found an increase of 18 year cardiac mortality with a Hazard Risk of 1.79.

Accurate interpretation of plasma hGH concentration is hampered by the fact that hGH is released in pulses over the majority of the day and in the morning hours, when plasma concentration is relatively stable {32}, {33}, {34}, hGH concentrations are low and sometimes undetectable using conventional hGH assays.

Summary

In an aspect, there is provided a method for predicting the cardiovascular risk or the total mortality risk within 10 years in a subject comprising: determining the fasting level of growth hormone (hGH), and/or its isoforms in a bodily fluid obtained from said subject; and correlating said fasting level of growth hormone (hGH), and/or its isoforms with a cardiovascular risk or the total mortality risk, wherein an enhanced level is predictive for an enhanced risk, wherein the cardiovascular risk is defined as an adverse event or the total mortality risk and wherein the risk of said adverse event or the total mortality risk is predicted within 10 years.

In another aspect, there is provided a ultra sensitive hGH assay comprising at least one monospecific binder, preferably two monospecific binders, having a binding affinity of 10^{-8}M or less to hGH and its isoforms and wherein said binder (s) is either specific for one of the secreted hGH isomers, or for more than one or is specific for and binds to all secreted isomers of hGH selected from the group comprising isomer 1, isomer 2, isomer 3 and isomer 4 (SEQ ID. NO: 1 to 4) and wherein ultrasensitive assay has an analytical assay sensitivity of less than 100 pg/ml, preferred less than 50 pg/ml, preferred less than 30 pg/ml, preferred less than 20 pg/ml, preferred less than 10 pg/ml, preferred less than 5 pg/ml, preferred 2 pg/ml. or a functional assay sensitivity of less than 400 pg/ml, preferred less than 200 pg/ml, preferred less than 120 pg/ml, preferred less than 80 pg/ml, preferred less than 40 pg/ml, preferred less than 20 pg/ml, preferred 10 pg/ml most preferred less than 8,5 pg/ml.

In yet another aspect, there is provided the use of an ultrasensitive hGH assay as defined herein in a method as defined herein.

Detailed Description

Subject matter of the present invention is a new ultra sensitivity assay for plasma hGH measurements (hGH), with accurate measurements also at low hGH plasma concentrations (*e.g.* assay sensitivity 2 pg/ml). Subject matter of the present invention is the correlation of the development of cardiovascular morbidity and mortality with hGH in fasted plasma in a subject. Subject matter of the present invention is the relation of hGH in fasted plasma in a subject and the risk of coronary artery disease (CAD), stroke, all-cause (total) mortality, and cardiovascular (CVD) mortality.

Subject matter of the present invention is a method for predicting the cardiovascular risk or the total mortality risk in a subject comprising: