CURRICULUM VITAE

Kim Claessen werd geboren als jongste van een tweeling op 24 maart 1989 te Roosendaal. Zij groeide op in Roosendaal in een gezin van vier kinderen, en bracht vele uren door op de tennisbaan verbonden aan de tennisschool Junior Top Tennis (JTT) van trainer Gillis van der Gruiter. Al sinds haar jeugd wist Kim dat zij dokter wilde worden. In 2007 behaalde zij *cum laude* haar Gymnasium diploma aan het Norbertus Lyceum, en begon zij aan de studie Geneeskunde aan de Universiteit Leiden. Zowel haar Propedeuse (2008) als Bachelor diploma (2010) werden *cum laude* behaald. Naast de tennistrainingen en –toernooien was Kim tijdens haar studententijd op vele andere fronten actief, en nam zij onder andere deel aan enkele Honours Classes, was zij snijzaal-assistent Anatomie en werkte zij als medisch triagist op de Huisartsenpost.

Reeds vroeg in haar studie Geneeskunde ontstond bij Kim de interesse voor wetenschappelijk onderzoek. In september 2009 werd zij geselecteerd voor het M.D./Ph.D.-traject voor Excellente Studenten, en startte zij vol enthousiasme met onderzoek aan de afdeling Endocrinologie en Metabolisme van het Leids Universitair Medisch Centrum (LUMC), onder leiding van Dr. N.R. Biermasz, Prof. Dr. M. Kloppenburg en Prof. dr. A.M. Pereira. Hiermee legde zij de fundering voor dit proefschrift. In april 2011, na de afronding van haar eerste 4 studiejaren van Geneeskunde en inmiddels verhuisd naar Amsterdam, ontving Kim van de Raad van Bestuur van het LUMC een 2-jarige beurs voor fulltime promotieonderzoek. In deze periode werden klinische studies bij patiënten met acromegalie en groeihormoondeficiëntie verricht. Daarnaast werden (genetische) studies uitgevoerd naar de rol van groeihormoon en IGF-1 bij primaire artrose, in samenwerking met de afdelingen Reumatologie en Moleculaire Epidemiologie van het LUMC. Tijdens haar onderzoeksperiode kreeg Kim de mogelijkheid een aantal cursussen op het gebied van Epidemiologie, Statistiek en Genetica te volgen, heeft zij meerdere posterpresentaties en mondelinge presentaties op nationale en internationale congressen gegeven, waarvoor haar enkele reisbeurzen werden toegekend.

In april 2013 is Kim gestart met haar coschappen aan het LUMC en zij zal in januari 2015 haar artsenbul in ontvangst nemen.

LIST OF PUBLISHED ABSTRACTS

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2. Claessen Kim, Kloppenburg Margreet, Kroon Herman, Bijsterbosch Jessica, Pereira Alberto, Romijn Hans, Van der Straaten Tahar, Beekman Marian, Slagboom Eline, Biermasz Nienke, Meulenbelt Ingrid. A functional growth hormone receptor polymorphism, exon 3 deleted GHR, is associated with radiographic knee osteoarthritis in females with familial osteoarthritis at multiple sites: the GARP Study. *Endocrine Reviews 2012*; 33: SUN-LB7.

3. Claessen KMJA, Kloppenburg M, Kroon HM, Bijsterbosch J, Pereira AM, Romijn JA, Van der Straaten T, Beekman M, Slagboom PE, Biermasz NR, Meulenbelt I. A functional growth hormone receptor polymorphism, exon 3 deleted GHR, is associated with radiographic knee osteoarthritis in females with familial osteoarthritis at multiple sites: the GARP Study. *Arthritis & Rheumatism 2012*; 64(10): S472-S473.

4. Claessen Kim, Appelman-Dijkstra Natasha, Pereira Alberto, Hamdy Neveen, Kroon Herman, Kloppenburg Margreet, Biermasz Nienke. Progression of vertebral fractures despite long-term biochemical control of acromegaly: a prospective follow-up study. *Endocrine Reviews 2013*; 34; FP27-6.

5. Claessen Kim, Kloppenburg Margreet, Kroon Herman, Bijsterbosch Jessica, Pereira Alberto, Romijn Johannes, van der Straaten Tahar, Nelissen Rob, Hofman Albert, Uitterlinden André, Duijnisveld Bouke, Lakenberg Nico, Beekman Marian, van Meurs Joyce, Slagboom Eline, Biermasz Nienke, Meulenbelt Ingrid. A functional growth hormone receptor polymorphism, exon 3 deleted GHR, is associated with osteoarthritis in females: the results of a meta-analysis. *Endocrine Reviews 2013*; 34: SAT-123.

6. Joustra Sjoerd, Claessen Kim, Appelman-Dijkstra Natasha, Dekkers Olaf, van Beek André, Wolffenbuttel Bruce, Pereira Alberto, Biermasz Nienke. High prevalence of metabolic syndrome features in patients previously treated for non-functioning pituitary macroadenoma. *Endocrine Reviews 2013*; 34: MON-104.

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1. Claessen KMJA, van Lieshout L, Visser LG. HIV and malaria co-infection: a Systematic Review. *JEMSA 2010*; 5: 1-11

2. Biermasz NR, van 't Klooster R, Wassenaar MJE, Malm SH, Claessen KMJA, Nelissen RGHH, Roelfsema F, Pereira AM, Kroon HM, Stoel BC, Romijn JA, Kloppenburg M. Automated image analysis of hand radiographs reveals widened joint spaces in patients with long-term control of acromegaly: relation to disease activity and symptoms. *European Journal of Endocrinology 2012*; 166 (3): 407-413

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4. Claessen KMJA, Ramautar SR, Pereira AM, Smit JWA, Roelfsema F, Romijn JA, Kroon HM, Kloppenburg M, Biermasz NR. Progression of acromegalic arthropathy despite long-term biochemical control: a prospective, radiological study. *European Journal of Endocrinology 2012*; 167 (2): 235-244. Comment in: *Nature Reviews Endocrinology 2012*; 8: 447 (Research Highlight)

5. Claessen KMJA, Appelman-Dijkstra NM, Adoptie DMMM, Roelfsema F, Smit JWA, Biermasz NR, Pereira AM. Metabolic profile in growth hormone deficient (GHD) adults after long-term recombinant human growth hormone (rhGH) therapy. *Journal of Clinical Endocrinology & Metabolism 2013;* 98 (1): 352-361
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8. Claessen KMJA, Kloppenburg M, Kroon HM, Bijsterbosch J, Pereira AM, Romijn JA, van der Straaten T, Nelissen RGHH, Hofman A, Uitterlinden AG, Duijnisveld BJ, Lakenberg N, Beekman M, van Meurs JB, Slagboom PE, Biermasz NR, Meulenbelt I. Relationship between the functional exon 3 deleted growth hormone receptor polymorphism and symptomatic osteoarthritis in women. *Annals of Rheumatic Diseases 2014;* 73(2): 433-436

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13. Claessen KMJA, Appelman-Dijkstra NM, Hamdy NAT, Pereira AM, Biermasz NR. Effects of up to 15 years of recombinant human GH (rhGH) replacement on bone metabolism in adults with Growth Hormone Deficiency (GHD): The Leiden Cohort Study. *Clinical Endocrinology 2014, in press*

14. Claessen KMJA, Meulenbelt I, Pereira AM, Kroon HM, Biermasz NR, Kloppenburg M. High serum insulin-like growth factor-1 (IGF-1) levels are associated with the presence of primary osteoarthritis, but not with radiographic progression: the GARP Study. *Submitted*

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17. Claessen KMJA, van Vliet NA, Verstegen MJ, Roelfsema F, Pereira AM, Biermasz NR. Long-term outcome of transsphenoidal surgery in acromegaly: The Leiden Cohort Study. *In progress*

18. Claessen KMJA, Biermasz NR, Mazziotti G, Giustina A. Bone and joint disorders in acromegaly. ***In progress***

APPENDICES

APPENDIX 1: Comment in Nature Reviews Endocrinology 2012; 8: 447 (Research Highlight) on 'Progression of acromegalic arthropathy despite long-term biochemical control: a prospective, radiological study (European Journal of Endocrinology 2012; 167(2): 235-244)'

pituitary function

Arthropathy in acromegaly

Long-term biochemical control of acromegaly does not prevent progression of acromegalic arthropathy in many patients, report researchers from The Netherlands.

Arthropathy is a complication of acromegaly that impairs quality of life both physically and psychologically. Cross-sectional studies had previously shown a high prevalence of arthropathy in patients with long-term biochemical control of acromegaly.

"However, the disease course of acromegalic arthropathy during prolonged follow-up is unknown in treated patients," explains lead author Kim Claessen of Leiden University Medical Center. "Therefore, the aim of the present study was to assess the course of acromegalic arthropathy in a cohort of long-term control patients and to identify potential risk factors for progression over 2.6 years of prospective follow-up."

The researchers studied 58 patients with acromegaly who had been in biochemical remission of the disease for a mean duration of 15 years. The investigators obtained radiographs of the knees, hips and hands of the patients at two study visits a mean interval of 2.6 years apart. Radiographic progression of arthropathy from baseline to follow-up was defined as a ≥1 point increase in the score for osteophytes or joint space narrowing according to the Osteoarthritis Research Society International atlas.

Radiographic progression of osteophytes and joint space narrowing at any joint site was observed in 42 (72%) and 43 (74%) patients, respectively. Surprisingly, patients whose disease was biochemically controlled by somatostatin analogues had a higher risk of osteophyte progression than patients cured by surgery or additional radiotherapy.

The findings might indicate insufficient control of growth hormone in patients treated with somatostatin analogues, the researchers suggest.

"Further studies, preferably randomized controlled trials, with longer follow-up duration are required to explore whether more aggressive treatment is beneficial for the outcome of acromegalic arthropathy," concludes Claessen.

Carol Wilson

Original article Claessen, K. M. *et al.* Progression of acromegalic arthropathy despite long-term biochemical control: a prospective, radiological study. *Eur. J. Endocrinol.* doi:10.1530/EJE-12-0147

APPENDIX 2: Comment in Reuters Health (2013, Nov 30th) on 'Metabolic profile in growth hormone deficient (GHD) adults after long-term recombinant human growth hormone (rhGH) therapy (Journal of Clinical Endocrinology and Metabolism 2013;98(1): 352-361)'

Long-term growth hormone treatment ups risk of metabolic syndrome

Nov 30, 2012 | Reuters Health News
By Anne Harding

NEW YORK (Reuters Health) – Adults with growth hormone deficiency (GHD) who take recombinant human growth hormone (rhGH) for 10 years or more are at increased risk of metabolic syndrome, a new study in 98 patients shows.

Given that improving cardiovascular risk is one of the major targets of rhGH therapy for adults with GHD, "the effects of long-term rhGH therapy on overall cardiovascular profile needs to be established in a larger GHD cohort and should also be compared to healthy controls to control for the effect of aging," Dr. Kim M. J. A. Claessen of Leiden University Medical Center in The Netherlands, one of the study's authors, told Reuters Health.

In the short term, the researchers note, rhGH therapy improves several cardiovascular risk factors, such as low-density lipoprotein (LDL) levels and body fat. However, they add, there is some evidence that rhGH therapy could actually increase cardiovascular risk.

To better understand the cardiovascular effects of long-term rhGH therapy in adults with GHD, the researchers looked at several efficacy parameters in patients who had been treated at their center for 10 years or longer. They recorded patients' data at baseline and after five, 10 and 15 years of therapy with rhGH, and reported the findings online November 15 in the Journal of Clinical Endocrinology and Metabolism.

The mean age of patients in the study was nearly 60 years. Total cholesterol and LDL cholesterol were significantly lower than at baseline, while high-density lipoprotein levels were higher, the researchers found. However, at 10 years, waist circumference, body mass index, and fasting plasma glucose levels were all higher than at baseline.

And the prevalence of metabolic syndrome nearly doubled, showing a greater increase than would have been expected based on aging alone. "This was mainly due to a gradual increase in abdominal obesity, hypertriglyceridemia, and hyperglycemia," the researchers wrote.

At baseline, 32.7% of patients had metabolic syndrome, while after 10 years on rhGH, 57.1% did. While men and women were equally likely to have the metabolic syndrome at baseline, the prevalence at 10 years was 44.9% in women and 69.4% in men.

"Since the profile of GHD patients changes over time, critical re-evaluation of the net benefit of long-term rhGH therapy is of paramount importance," Dr. Claessen said via email. "Therefore, at present, the indication for long-term rhGH therapy should be established in every individual patient, and critically be re-evaluated during long term treatment."

It is also important to look at the cost-benefit ratio of rhGH therapy compared to other widely available medications, such as statins, that have proven effectiveness in secondary cardiovascular risk prevention, the researcher added.

SOURCE: Journal of Clinical Endocrinology and Metabolism, online November 15, 2012.

APPENDIX 3: Comment in: Lancet Diabetes & Endocrinology 2013 (Research in Brief) on 'Progression of vertebral fractures despite long-term biochemical control of acromegaly: a prospective follow-up study (Journal of Clinical Endocrinology and Metabolism 2013, in press)'

Progressive vertebral fractues in acromegaly

Written by Iley Ozerlat-Gunduz

In a prospective study including 49 patients with mean age of 61.3±11.1 years having controlled acromegaly for a mean of 17 years the natural course of vertebral fractures was assessed over a follow-up of 2.5 years. Remission of acromegaly was achieved by surgery, radiotherapy and/or medical therapy and patients did not use bisphosphonates. In these patients, baseline prevalence of vertebral fractures was 63%, and at the end of the follow up period, progressive fractures were found in 20% of patients despite adequate biochemical remission of acromegaly. Progression rate was highest in patients with 2 or more fractures at baseline and in men, but was independent of bone mineral density.

The data of the present study suggest that despite long-term biochemical remission acromegaly patients are at risk for progressive vertebral fractures, indicating persisting abnormalities in bone quality in these patients, possibly related to pretreatment long-term exposure to high circulating levels of GH. Further research has to elucidate the pathophysiological basis of the changes in bone quality leading to the high vertebral fracture risk and whether acromegaly patients require treatment for these fractures.

PA/PA Archive/Press Association Images

Her Majesty the Queen views the skeleton of Charles Byrne (1761–83), an Irish-born man who had acromegaly