CONgenital CORvitia

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National registry and DNA-bank of adults with congenital heart disease

Number of participating hospitals: 103

Number of included patients: 11,433

Project group: BJM Mulder, AMC Amsterdam; ET van der Velde, LUMC Leiden; J Vis, ICIN; CJM Engelfriet-Rijk, ICIN; I Harms, ICIN; S Mantels, ICIN

Steering committee: BJM Mulder, chairman, ICIN; ET van der Velde, LUMC Leiden; ECM Mariman, AZM Maastricht; FJ Meijboom, UMC Utrecht; HW Vliegen, LUMC Leiden; G Veen, VUMC Amsterdam; PG Pieper, UMC Groningen; HWM Plokker, St Antonius Hospital Nieuwegein; APJ van Dijk, Radboud UMC Nijmegen; JLM Stappers, AZM Maastricht; JW Roos-Hesselink, EMC Rotterdam; JGP Tijssen, AMC Amsterdam; RMF Berger, UMC Groningen; GJ Sieswerda, UMC Utrecht

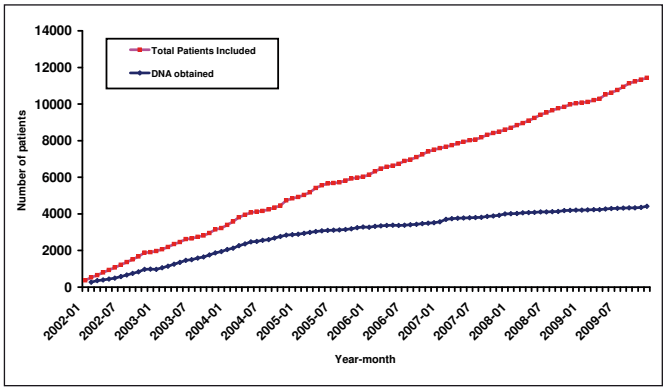

Figure 1. Progress of inclusion.

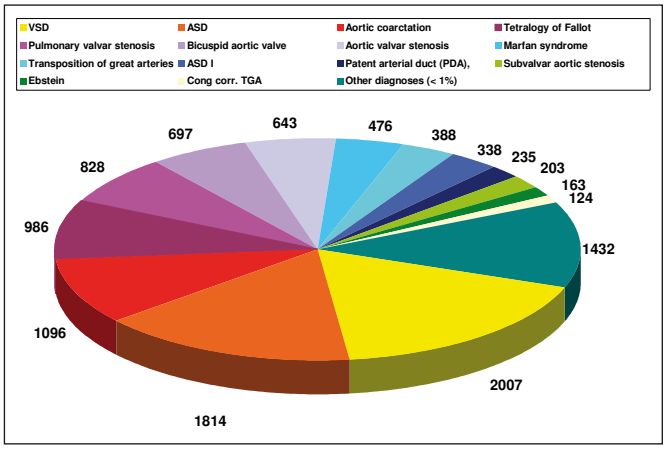

Figure 2. Most frequent main diagnoses

ZAHARA II

Pregnancy in adult congenital heart disease

A prospective, international multi-centre cohort study to examine the cardio-uterine interaction in pregnancy of women with congenital heart disease (CHD). Women with CHD presenting <20 weeks of pregnancy duration can be included.

Start of study: 1 March 2008
Planned inclusion: 160 pregnant women with CHD, and 60 healthy pregnant women
Number of included patients: 157
Number of included controls: 33
30 November 2009

Study coordination: A Balci, ICIN, Utrecht; Department of Cardiology, UMCG, Groningen, the Netherlands.
Project leaders: PG Pieper, Department of Cardiology, UMCG, Groningen
JG Aarnoudse, Department of Obstetrics & Gynaecology UMCG, Groningen
Principal investigators: The Netherlands: Department of Cardiology: PG Pieper, UMCG, Groningen; BJM Mulder, AMC, Amsterdam; JW Roos-Hesselink, Erasmus MC, Rotterdam; APJ van Dijk, UMCN St. Radboud, Nijmegen; HW Vliegen, LUMC, Leiden; E Wajon, MST, Enschede; JLM Stappers, AZM, Maastricht; GJ Sieswerda, UMCU, Utrecht; G Veen, VUMC, Amsterdam. Department of Obstetrics & Gynaecology: JG Aarnoudse, KM Sollie, UMCG, Groningen.
Belgium: Department of Cardiology: W Budts, UZL, Leuven, Department of Obstetrics & Gynaecology: M. Hanssens, UZL, Leuven

For information or inclusion of patients, please contact us at: a.balci@thorax.umcg.nl

Uteroplacental flow and complications in women with CHD

Pregnancy-induced hypertension and preeclampsia are the most important obstetric complications in pregnancies of women with CHD, whereas intrauterine growth restriction (IUGR), preterm delivery, and offspring mortality are the main complications in offspring. The magnitude of these risks depends on the type and severity of maternal CHD. An important common denominator in the pathophysiology of these complications is an inadequate uteroplacental circulation. In preeclampsia and intrauterine growth restriction several anatomical changes in the placental bed have been described. Different studies have shown that deterioration of uterine artery Doppler flow patterns (abnormal pulsatility index and persistent diastolic notching) are associated with impaired placental perfusion and poor pregnancy outcome. Uterine artery screening also significantly predicts recurrence of poor pregnancy outcome in high-risk populations. In addition, abnormal flow velocity waveforms of umbilical arteries are also associated with a poor pregnancy outcome. These now mainstream noninvasive simple ultrasound techniques, therefore, may prove useful in the (early) identification of high-risk pregnancies in CHD patients. In ZAHARA II we prospectively study the changes in cardiac parameters and in uteroplacental flow parameters in pregnant women with CHD and in healthy controls, and relate these to the occurrence of cardiac, obstetric and neonatal complications. ■

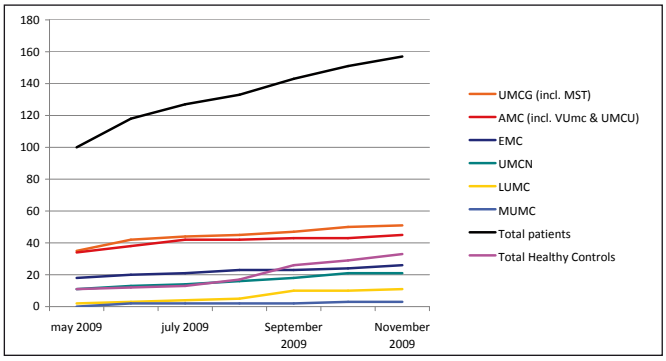

Figure 1. Distribution of included patients and healthy controls in ZAHARA II.

RACE 3

Number of included patients: 15
1 December 2009

This study is supported by: Biotronik, Boehringer Ingelheim, Boston Scientific, Medtronic, Sanofi Aventis, St. Jude Medical and Astra Zeneca.

Steering committee: Isabelle C. Van Gelder, UMC Groningen; Marco W. Alings, Amphia Hospital Breda; Harry J.G.M. Crijns, Maastricht UMC; Raymond Tukkie, Kennemer Gasthuis Haarlem; Johan Brügemann, UMC Groningen; Joep R.L.M. Smeets, UMC Nijmegen; Charles J.H.J. Kirchhof, Rijnland Hospital, Leiderdorp; Hans L. Hillege, UMC Groningen; Jan G.P. Tijssen, AMC Amsterdam; Dirk J. Van Veldhuisen, UMC Groningen, Robert G. Tieleman, Martini Hospital Groningen
Study coordination: Marcelle D. Smit, UMC Groningen
PhD Student: Ismaël D. Achekar, UMC Groningen

As of 1 December 2009, the Oosterschelde Hospital Goes, Amphia Hospital Breda, Rijnstate Hospital Arnhem/Velp, ZGT Hospital location Almelo, Kennemer Gasthuis Haarlem and the University Medical Center Groningen have been initiated to start the inclusion of patients for the RACE 3 study. De Tjongerschans Hospital and MC Haaglanden will follow this month. On 1 December 2009 a total of 15 patients had been included in the trial. Below you will find a picture of the presentation of the Race 3 study in the foyer of the Dutch Network for Cardiovascular Research (WCN) congress 2009 in Amsterdam. ■

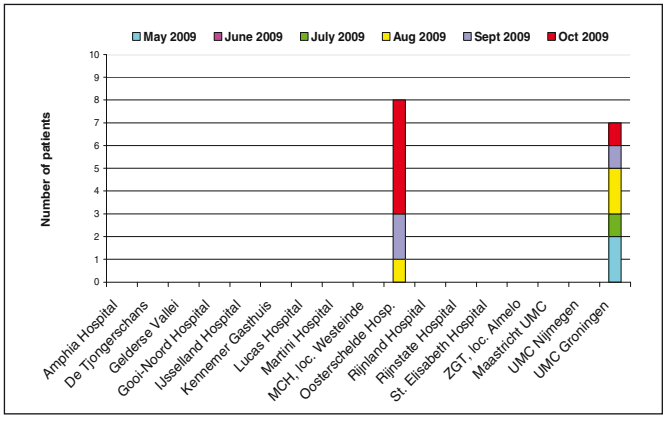

Figure 1. Patients included in RACE 3.
Figure 2. WCN Congress 2009.

HEBE III

A prospective, randomised, clinical study to examine the effects of a single bolus of erythropoietin on left ventricular function in patients with a myocardial infarction

Number of included patients: 529
1 June 2009

Funded by the Netherlands Heart Foundation

Study coordination: A. Belonje, UMC Groningen

Principal investigators: A.A. Voors, F. Zijlstra, D.J. van Veldhuisen, UMC Groningen

Participating centres: University Medical Center Groningen, University Medical Center Leiden, Medical Centre Alkmaar, Isala Clinics Zwolle, Amphia Hospital Breda, Academic Medical Center Amsterdam, St. Antonius Hospital Nieuwegein

Safety issues concerning erythropoietin treatment

The HEBE III study design was primarily based on experimental studies and a few small clinical trials.[1] We performed a safety study including 22 patients with an acute myocardial infarction (AMI), and from these results we could conclude that an intravenous single high-dose of erythropoietin after AMI was well tolerated and safe.[2]

In the inclusion phase of the HEBE III trial, a safety analysis was performed by the Data Safety Monitoring Board (DSMB) and they concluded that there were no safety problems. However, during the course of the study, a few articles were published on the use of erythropoietin in patients with chronic kidney disease (CKD) and patients with stroke. The results of these studies were reason for some safety questions concerning the use of erythropoietin in these patient groups. Two studies evaluating the effect of erythropoietin treatment for increasing haemoglobin to normal levels in patients with CKD failed to demonstrate a better survival.[3,4] Furthermore, a recently published study by Ehrenreich et al.[5] showed no favourable effects of erythropoietin treatment in ischaemic stroke patients. In fact, this study raised some safety concerns about the use of erythropoietin in this population, since the overall death rate in the erythropoietin group was almost twice as high as in the control group. These results were of course discussed with our Central Medical Ethics Committee and because the aforementioned studies concerned different patient groups than our group and the DSMB failed to show any safety concerns in the HEBE III study, there was no reason to stop our study prematurely. ■

References

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2 Lipsic E, van der Meer P, Voors AA, Westenbrink BD, van den Heuvel AF, de Boer HC, et al. A single bolus of a long-acting erythropoietin analogue darbepoetin alfa in patients with acute myocardial infarction: a randomized feasibility and safety study. Cardiovasc Drugs Ther. 2006;20:135-41.
3 Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med. 2006;355:2085-98.
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5 Ehrenreich H, Weissenborn K, Prange H, Schneider D, Weimar C, Wartenberg K, et al. Recombinant Human Erythropoietin in the Treatment of Acute Ischemic Stroke. Stroke. 2009;40:e647-56.

GENetic CORvitia

National registry for patients and families with a familial heart disease

www.gencor.nl

Number of included patients: 1578
30 October 2009

Project leaders: Y.M. Pinto, ICIN; A.A.M. Wilde, ICIN

Project coordination: J.F. Hermans-van Ast, ICIN

Steering committee: Y.M. Pinto, chairman, ICIN; A.A. Wilde, chairman, ICIN; I. Christiaans, AMC Amsterdam; J.P. van Tintelen, UMC Groningen; D.E. Atsma, LUMC Leiden; Y.H. Arens, MUMC Maastricht; C.L. Marcelis, UMCN Nijmegen; M. Michels, EMC Rotterdam; J.J. van der Smagt, UMC Utrecht; A.C. Houweling, VUMC Amsterdam

In GENCOR, patients with familial heart diseases are registered. One of these diseases is the Brugada syndrome (BrS). BrS is a disease that features characteristic right precordial ST-segment elevations and (discrete) signs of conduction slowing in all cardiac compartments in conjunction with an increased risk of sudden cardiac death. The typical clinical manifestation is nocturnal sudden death in males at the age of around 40. Hyperthermia may be a precipitating factor. Also, there is an increasing number of case reports of drug-induced ST-segment changes. These drugs should be avoided by patients with BrS (www.brugadadrugs.org). At present, seven potentially causal genes have been identified. The mode of inheritance is autosomal dominant.
Figure 1 gives an overview of the location of almost all mutations found in the *SCN5A* gene in the Netherlands, the most important gene associated with BrS. In the past period, inclusion of patients with hypertrophic cardiomyopathy was emphasised in GENCOR. That is why the number of included families with BrS in GENCOR is limited. In GENCOR 30 patients (divided over 14 families) are registered with a mutation in the *SCN5A* gene. Three mutations are reported in two or three families. ■

Acknowledgement
Thanks to Mariel Alders and Andre Linnenbank of the Academic Medical Center for preparing the figure.

Reference
www.cardiogenetica.nl

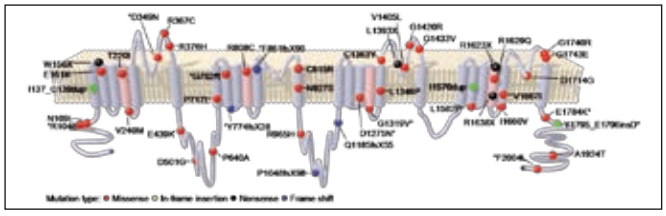

Figure 1. Location of mutations in the SCN5A gene. The mutations marked with an asterisk are reported in GENCOR.