Funding: German Foundation for Heart Research (Deutsche Stiftung für Herzforschung)

Funding Patient-Oriented Cardiovascular Research

Recipients of German Foundation for Heart Research (Deutsche Stiftung für Herzforschung) grants in 2012 describe the funding and their research to Jennifer Taylor, BSc, MSc, MPhil.

Creation of a Multicentre Database to Evaluate the Use of Pacemakers and Defibrillators in Paediatric Patients with Congenital Heart Diseases

Peter A. Zartner, MD, FESC, paediatric cardiologist and medical computer scientist, German Paediatric Heart Centre, Sankt Augustin, Germany, received €10,000 from the German Foundation for Heart Research (see www.dshf.de) in 2012 to evaluate the use of pacemakers and defibrillators in paediatric patients with congenital heart diseases.

Current use of pacemakers in infants and children has been adapted from techniques and material used for adults, but paediatric patients require different and individual strategies for in- and ex-plantation procedures, programming and tracing of the systems, adaptation to a variety of anatomical malformations, and coordination with interventional or surgical procedures. Paediatric restrictions and changes over time, such as vessel diameter and patient’s growth, must be considered. The levels of evidence in the American Heart Association, American College of Cardiology, and Heart Rhythm Society guidelines for device-based therapy for patients with congenital heart diseases are C, with an increasing number of B, which reflects the necessity of an extended and comprehensive data analysis in this patient group.

To address the lack of information, Dr Zartner’s project aims to retrospectively analyse the use of electronic pacing systems in paediatric patients over the past 20 years in a multicentre setting. An internet-based, relational database is being created using patient data from the different centres, especially concerning implanted material and implantation strategies (eg, epimyocardial vs transvenous) in relation to a patient’s age, size, heart defects, and clinical problems to determine which parameters provide information on the quality of pacemaker therapy. Computer-based statistical evaluation of this database isolates the most common problems and complications. All parameters will be assessed to optimise the runtime of the implanted systems and reduce the frequency of revisions. Dr Zartner says, “We hope to gain new insights into foreseeable problems with implantable electronic devices in paediatric practice to optimise strategies for pacemaker therapy in children.”

On other pages...

- **Awards: Women and Heart Research Prize**
  A research prize of CHF 30,000 awarded to researchers or research groups in Switzerland for projects that have cardiovascular disease in women as their main focus.  
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- **European Meetings Update, 1 to 29 May, 2013**
  List of cardiovascular meetings in Europe taking place from May 1 to May 29, 2013.  
  Page f66
We also want to gather a collection of bail-out procedures in pacemaker therapy in children.”

Essential support in initiating and conducting the project has been provided by the Department of Paediatric Cardiology, Friedrich-Alexander University of Erlangen-Nürnberg. The project is coordinated by the government-funded Kompetenzzentrum Angeborene Herzfehler (Competence Network for Congenital Heart Defects) in Berlin, Germany. Departments of Paediatric Cardiology that have agreed to participate so far are those based at Friedrich-Alexander University of Erlangen-Nürnberg; the Heart Centre of the University of Leipzig, Leipzig, Germany; the German Paediatric Heart Centre, Sankt Augustin, Germany; the West-German Heart Centre, University of Essen, Essen, Germany; and the German Heart Centre, Berlin, Germany.

Before receiving the grant, Dr Zartner conducted clinical research on pacemaker therapy in children, new strategies in coronary interventions in children, the use of biodegradable magnesium stents in newborns, the use of stents in pulmonary arteries and arterial ducts in infants, and interventional closure of interatrial communications with different devices. He says, “Hopefully, receiving the German Cardiac Research Foundation 2012 research grant will help us gain valuable information for treating our patients and boost future research grant applications.”

References

Investigating Stress and Responses to Stress in Patients with Transient Left Ventricular Apical Ballooning Syndrome

Sabrina Kastaun, Dipl Psyeh, psychologist, and Mesut Yeniguen, MD, neurologist, Heart and Brain Research Group, Department of Neurology, Justus-Liebig-University Giessen, Giessen, Germany, and Kerckhoff Clinic Bad Nauheim, Bad Nauheim, Germany, received a German Foundation for Heart Research grant of €60,000 in 2012 over 21 months to investigate patients with stress (takotsubo) cardiomyopathy in terms of personality traits, stress management, and psychopathological predisposing factors.

Stress-induced cardiomyopathy, also referred to as transient left ventricular apical ballooning syndrome (TLVAB) is a recently described disease mimicking acute myocardial infarction. It presents with acute chest pain and dyspnoea, accompanied by ST-segment elevation and/or T-wave inversion in the electrocardiogram, elevation of cardiac enzyme levels, and transient wall motion abnormalities in the left ventricle mid-segments in the absence of obstructive coronary disease. Its prevalence among patients with suspected acute myocardial infarction varies between 0.7% and 2.5%. Although systolic dysfunction mostly recovers within a few weeks, the inhospital mortality rate is 2%.2

The aetiology of TLVAB is not fully understood. Possible theories include ischaemia-mediated stunning caused by multivessel epicardial or microvascular spasm and myocarditis. An elevated release of catecholamines seems to play a key role. A theory of catecholamine-mediated myocardial stunning provoked by emotional or physiological stress is supported by increased plasma catecholamine measurements during the acute phase in >70% of patients.3 Interestingly, TLVAB predominantly occurs in postmenopausal women, typically during an emotionally or physiologically stressful event (eg, bereavement, arguments, surgery, severe pain). No stressful trigger is observed in one-third of patients.2

Psychological approaches to understanding the aetiology of TLVAB have not yet been applied. However, with funding from the German Foundation for Heart Research, Ms Kastaun and Dr Yeniguen will address this by investigating the relationship between TLVAB and premorbid psychiatric disorders, certain personality traits, and/or excessive susceptibility to stress. Their case-control study assesses the presence of chronic stress, stressful life events, stress management strategies, personality traits, locus of control (internal, external), and the presence and pattern of psychiatric symptoms in female patients diagnosed with TLVAB at Kerckhoff Clinic Bad Nauheim within the past 4 years.

Female patients with a previous history of non–ST-segment elevation myocardial infarction serve as 1 control group. A second control group of cardiac-healthy women is drawn from the general population. Both control groups are matched for age, and the non–ST-segment elevation myocardial infarction group is also matched for the index event date.

In a self-designed stress experiment, the researchers will also measure salivary cortisol to determine patients’ stress reaction pattern and the general vulnerability to stress for each group. Measurement of neuroendocrine markers, such as free cortisol in saliva, has proved useful for assessing functioning and reactivity of the hypothalamic–pituitary–adrenal axis in psychological stress tasks.4
Ms Kastaun says, “The study aims to determine the role of personality traits, stress management, and psychopathological predisposing factors in the pathogenesis of stress cardiomyopathy.”

The Heart and Brain Research Group is a joint venture between the Department of Neurology of the Justus-Liebig-University Giessen and the Departments of Cardio-surgery and Cardiology of the Kerckhoff Clinic in Bad Nauheim. Since 2000, their work has focused on neurological and neuropsychological aspects of heart diseases and cardiac surgery, including clinical and preclinical approaches. Dr Reniguen concludes, “The interdisciplinary philosophy of our group will hopefully provide innovative scientific approaches that help us to understand the complex pathophysiology of stress-induced cardiomyopathy.”

References

Investigating Platelet Function in Patients with Acute Coronary Syndrome Treated with Mild Hypothermia

Jan Kaufmann, MD, cardiologist, Department of Internal Medicine, Cardiology, German Heart Institute Berlin, Berlin, Germany, received €30,000 from the German Foundation for Heart Research in 2012 for 1.5 years to assess platelet function in patients with acute coronary syndrome treated with mild hypothermia.

Therapeutic hypothermia has been demonstrated to improve outcomes for patients with acute coronary syndrome.1 The highest risk for stent thrombosis occurs within the first 48 hours after percutaneous coronary intervention, so quick and sufficient inhibition of platelet function is crucial to avoid thrombembolic complications. However, previous data point to an interaction between hypothermia and drug metabolism, thus potentially impacting on platelet function under antiplatelet therapy.2

Dr Kaufmann’s study involves close cooperation between the Deutsches Herzzentrum Berlin and the Department of Nephrology/Intensive Care Medicine, Charité University Hospital Berlin (Campus Virchow). The study tutor at the Charité site is Christian Storm, MD. Following resuscitation and revascularisation by percutaneous coronary intervention, patients with acute coronary syndrome are subjected to mild hypothermia (33°C) in accordance with current guidelines for 24 to 48 hours using a noninvasive feedback surface cooling device. All patients in the study receive routine thienopyridine treatment with clopidogrel.

Previous ex vivo analysis of platelet function suggests increased platelet reactivity in mild hypothermia compared with normal body temperature, indicating an attenuated clopidogrel response.3 Clopidogrel is a prodrug activated by hepatic cytochrome P450. This involves an intermediate activation step leading to the generation of 2-oxo-clopidogrel, followed by a final oxidative step resulting in the active metabolite. Cytochrome P450 P2C19 has been demonstrated to contribute up to 45% of the initial and 20% of the final clopidogrel prodrug activation. Alterations in biotransformation in hypothermia may impact active drug levels. Platelet function might also be affected by hypothermia, leading to a diminished antiplatelet effect. Thus, hypothermia may also influence action of more novel P2Y12 ADP-receptor antagonists, such as prasugrel and ticagrelor.

To discriminate a pharmacokinetic from a pharmacodynamic impact, platelet function is tested ex vivo under conditions of mild therapeutic hypothermia (33°C) and normal body temperature. Different devices that highlight several aspects of platelet aggregation are used to assess platelet function. The control group comprises patients with acute coronary syndrome and percutaneous coronary intervention but not needing hypothermia. Clopidogrel metabolites are measured, and patients are screened for genetic determinants of clopidogrel metabolism.

Dr Kaufmann says, “This combination of clinical and basic science will help to identify the impact of hypothermia on platelet function and thus identify patients with an increased risk for thrombembolic complications.” He adds, “The support of the German Foundation for Heart Research enables independent project management and because the financial support is provided by a notable foundation, it has a positive impact on the career of all participants. Furthermore, it facilitates cooperation projects and encourages continuing interdisciplinary research.”

References

Jennifer Taylor is a freelance medical journalist.
To encourage cardiovascular research in women, the Olten Heart Foundation, a branch of the Swiss Heart Foundation, decided to launch the research prize “Women and Heart” in 2007.

Although clinically manifested disease develops 7 to 10 years later in women than in men, cardiovascular disease is the major cause of death in women >65 years of age, yet women are underrepresented in research in many important areas of cardiology. The mean percentage of women enrolled in cardiovascular clinical trials since 2006 has been 30%, and only 50% of trials report results by gender analysis. Less evidence-based preventive, diagnostic, and therapeutic options for women with cardiovascular disease may lead to undertreatment and a lower quality of care compared with men. Moreover, female-specific issues related to pregnancy and hormonal changes during menopause need more attention.1

The “Women and Heart” research prize of CHF 30,000 is awarded to researchers or research groups in Switzerland for research projects that have cardiovascular disease in women as their main focus.

The scientific committee that decides the winner is composed of leading academic staff from 3 Swiss University Hospitals and Olten Heart Foundation board members. Since the first call for applications, 5 distinguished researchers have been awarded the prize. Each year, the award round is announced at Swiss university hospitals and in the Swiss medical press. The deadline for submission of new projects for the 2013 prize is 27 May 2013.

The 3 most recent winners of the “Women and Heart” research prize are Nicole Aebischer, MD, head, Outpatient Cardiology Clinic, University Hospital Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, in 2010 for her project titled “Menopausal Women with Peripheral Artery Disease and Cardiovascular Risk Factors: Prevalence of Coronary Artery Disease”; Professor Elisabeth Zemp Stutz, MD, MPH, PhD, unit leader Society, Gender, and Health, Swiss Tropical and Public Health Institute, Basel, Switzerland, in 2011 for her project titled “Menopausal Women with Peripheral Artery Disease and Cardiovascular Risk Factors: Prevalence of Coronary Artery Disease”; and Petra Stute, MD, PD, deputy head, Department of Gynaecological Endocrinology and Reproductive Medicine and head, Menopause Clinic, University Women’s Hospital Inselspital Bern, Bern, Switzerland, in 2012 for her research project, “Is There a Window of Opportunity for Coronary Heart Disease Prevention in Swiss Women?”

From left to right: Dr Aebischer, MD, winner of the Women and Heart prize in 2010; Professor Stutz, winner of the Women and Heart prize in 2011; Julia Dratva, MD, MPH, Professor Stutz’s scientific collaborator at the Swiss Tropical and Public Health Institute. Photographs courtesy of Dr Aebischer and Professor Stutz.
2012 Winner: Investigating Effect of Hormone Replacement Therapy Started Within 6 Years of Menopause on Occurrence and Severity of Acute Coronary Syndrome

Basic science and observational studies suggest that oestrogens protect against coronary heart disease. However, the Women’s Health Initiative failed to prove this hypothesis. One explanation for this lack of benefit and the increase in coronary heart disease risk observed in the Women’s Health Initiative may derive from the harmful effects of hormone replacement therapy in older women. In contrast, younger post-menopausal women seem to benefit from oestrogen therapy. A timing hypothesis has been postulated, with exogenous oestrogens having beneficial cardiovascular effects when administered soon after endogenous oestrogen deficiency before significant atherosclerosis has developed, but having no or deleterious effects when given later.

The aim of Dr Stute’s study is to test whether hormone replacement therapy started within 6 years of menopause delays a first acute coronary syndrome and/or decreases its severity. A total of 4827 women with a first acute coronary syndrome event have been recorded in the database of the Department of Cardiology Inselspital Bern between 1995 and 2010. These women will be contacted by mail, and those who then volunteer for the study will be contacted for a telephone interview. The interview will address reproductive history, exogenous hormone exposure (hormonal contraception, hormone replacement therapy), and psychosocial stress factors preceding the acute coronary syndrome event.

The goal is to recruit ≈1500 women. Information on cardiovascular risk factors will be extracted from medical records. Risk parameters are likely to change due to treatment effects. Statistical analysis will therefore take into account dynamic modelling of the hazard function.

During the project, Dr Stute will be assisted by 3 medical students to conduct the telephone interviews as part of their doctoral theses. In addition, she has 2 coworkers with statistical expertise: Prisca Eser, PhD, research assistant, Department of Cardiovascular Prevention and Rehabilitation, Inselspital Bern, and Winfried Stute, PhD, professor of statistics and theory of probability, Institute of Mathematics, Justus-Liebig University Giessen, Giessen, Germany.

Dr Stute, who is originally from Germany, moved to Switzerland for her current position in 2009. She has since collaborated with the Department of Cardiovascular Prevention and Rehabilitation, Inselspital Bern.

Previously, Dr Stute’s scientific focus on the menopause and postmenopausal hormone replacement therapy has mainly concerned its effect on the breast. To help her make the transfer to cardiovascular research, she has undergone postdoctoral research training at the Primate Center, Department of Comparative Medicine, Wake Forest University School of Medicine in Winston Salem, NC, a well-known research centre for cardiovascular health with Professor Thomas B. Clarkson, DVM.

“The results of the study may justify hormone replacement therapy when prescribed correctly to prevent coronary heart disease if a delay in first acute coronary syndrome event or a decrease in acute coronary syndrome severity can be shown for a particular hormone replacement therapy group,” says Dr Stute.

“The potential long-term effect of this study may include coronary heart disease mortality reduction in women. Thus, on the public health level, we are investigating whether hormone replacement therapy may reduce the economic burden in our healthcare system by decreasing the incidence of coronary heart disease and/or its severity with probably a reduction (oestrogen only therapy) or null effect (oestrogen-progestogen therapy) on breast cancer risk, respectively.”

References

Jennifer Taylor is a freelance medical journalist.
European Meetings Update

1 to 31 May, 2013

2 to 5 May
The Heart and Beyond: Intercellular and Interorgan Communication
Varefana, Italy
For further details, see http://www.escardio.org/communities/Working-Groups/myofunction/meetings/

3 to 4 May
EuroValve Congress
Ibiza, Spain
For further details, see http://www.eurovalvecongress.com

5 to 8 May
ICNC 11, Nuclear Cardiology and Cardiac CT
Berlin, Germany
For further details, see http://www.escardio.org/congresses/ICNC11

6 to 9 May
ESC Webinar on Diabetes and Heart Disease
Online, France
For further details, see http://www.escardio.org/education/eLearning/webinars/

8 to 10 May
The Role of Advanced Cardiac Imaging: Clinical Decision Making in Coronary Artery Disease
Venice, Italy
For further details, see http://www.escardio.org/communities/EACVI/congress-meetings/Pages/Role-Advanced-Cardiac-Imaging

8 to 11 May
Annual Meeting of the Hungarian Society of Cardiology
Balatonfured, Hungary
For further details, see http://www.mkardio.hu

16 to 18 May
The International Cardiology Symposium—A Global Agenda (ICS-13),
Dubai, United Arab Emirates
For further details, see www.ics2013.com

16 to 18 May
Annual Meeting of the Danish Society of Cardiology 2013
Nyborg, Denmark
For further details, see http://www.cardio.dk

17 to 18 May
4th Georgian Congress of Cardiology
Tbilisi, Georgia
For further details, contact cardio@geosc.ge

20 to 24 May
Hammersmith Echocardiology Conference 2013
London, United Kingdom
For further details, see http://www.w12conferences.co.uk/w12-event-calendar

21 to 24 May
EuroPCR 2013
Paris, France
For further details, see http://www.escardio.org/congresses/EuroPCR

22 to 25 May
Association for European Paediatric and Congenital Cardiology (AEPC 2013)
London, United Kingdom
For further details, see http://www.aepc-2013.org

23 to 25 May
EuroCMR 2013
Florence, Italy
For further details, see http://eurocmr2013.medconvent.at/

23 to 25 May
Cardiac Nuclear and CT Imaging in Clinical Practice
Sophia Antipolis, France
For further details, see http://www.escardio.org/education/live-events/courses/nuclear-cardiology

24 to 24 May
New Recommendations for ST-Elevation Myocardial Infarction Management
Online, France
For further details, see http://www.escardio.org/education/eLearning/webinars

24 to 25 May
Brugada Symposium: 20 Years of Scientific Progress
Brussels, Belgium
For further details, see http://www.brugada-symposium.com/

25 to 28 May
Heart Failure 2013
Lisbon, Portugal
For further details, see http://www.escardio.org/congresses/hf2013

28 to 29 May
First International Symposium on Vascular Tissue Engineering
Leiden, The Netherlands
For further details, see http://www.vascular-tissue-engineering.org

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