Tetralogy of Fallot is the most common cyanotic heart defect at birth, accounting for ≈10% of all congenital cardiac defects. Early surgical repair has dramatically improved its outcome, but serious late complications remain of concern, in particular sudden cardiac death. A recent article in Circulation examined how left ventricular longitudinal function predicts life-threatening ventricular arrhythmia and death in adults with repaired tetralogy of Fallot.1

“Accurate risk stratification and the development of appropriate algorithms for the selection of patients who may benefit from an implantable cardioverter-defibrillator would be crucial in this context,” says the last author of this article, Helmut Baumgartner, MD, FACC, FESC, professor of cardiology/adult congenital heart disease, University of Muenster, Muenster, Germany, and director, Division of Adult Congenital and Valvular Heart Disease, Department of Cardiovascular Medicine, University of Muenster.

Previous studies have focused on the predictive value of surgical history, electrocardiographic variables, inducible arrhythmia, exercise intolerance, and right ventricular burden of myocardial fibrosis. More recently, left ventricular systolic dysfunction and diastolic dysfunction have been reported to carry prognostic information in this setting.

Professor Baumgartner explains that although left ventricular impairment is not uncommon in patients with tetralogy of Fallot, few patients present with more than mildly reduced left ventricular ejection fraction. Therefore, more sensitive measures of early left ventricular dysfunction may be required.

The study on left ventricular longitudinal function was carried out in collaboration with the Royal Brompton Hospital, London, England, to assess its prognostic value and incremental value compared with established predictors of outcome in a large cohort of patients with tetralogy of Fallot. Professor Baumgartner’s colleagues, Gerhard-Paul Diller, MD, PhD, FESC, and Aleksander Kempny, MD, played a key role.

Professor Baumgartner says, “The major findings of the study were that left ventricular longitudinal dysfunction was associated with a higher risk of sudden cardiac death and life-threatening arrhythmias in contemporary patients with tetralogy of Fallot. This study may prove to be a significant step forward in the risk assessment of patients with tetralogy of Fallot.”
Professor Baumgartner in the cath lab during an intervention. Photograph courtesy of Professor Baumgartner.

“Some Key Articles Resulted from this Work Describing Localised High Velocities and Pressure Recovery as a Source of Major Discrepancy between Doppler Measurements and Direct Haemodynamic Assessment”

Professor Baumgartner was born in St. Poelten, Austria, and graduated from the University of Vienna Medical School, Vienna, Austria, in 1981. During postgraduate training at the Krankenhaus der Barmherzigen Schwestern, Linz, Austria, and St. Poelten General Hospital, he spent a year from 1989 to 1990 as a research fellow funded by a Schrödinger research grant in the Division of Cardiology, Cedars-Sinai Medical Center, University of California, Los Angeles, CA, where he was mentored by Professor Gerald Maurer, MD, FESC, FACC. This experience was a major step in the development of his career, and his “productive year” has led to ongoing collaboration and repeat visits. Professor Baumgartner then returned to Linz and completed his clinical fellowship in cardiology in 1991.

Professor Baumgartner’s fascination for the heart developed during anatomy lessons at medical school. A “charismatic Austrian cardiologist and outstanding teacher,” Professor Peter Kuehn, MD, then encouraged him to pursue a career in cardiology. “Professor Kuehn was a leading cardiologist in Austria and part of the founding generation of cardiology in the country,” says Professor Baumgartner. “As an outstanding teacher, excellent physician and scientist, and distinguished personality whom I still admire, he had a particular influence on my career and personal development. To train with him and receive his ongoing support was definitely the solid basis for my career.” At this time, “the golden days of echocardiography,” when 2-dimensional echocardiography was becoming established and Doppler techniques were appearing on the horizon, but with uncertain clinical impact and validity, Professor Baumgartner says, “I had the great opportunity to enter an exciting new and rapidly developing field. My fascination for valvular and congenital heart disease was ideal for delving deeply into this area, both clinically and scientifically.” As a result, Professor Baumgartner gathered extensive clinical experience and participated in new diagnostic and therapeutic approaches when structural heart disease was receiving little general attention in cardiology.

Having already started research into the development and validation of echocardiographic and Doppler techniques to diagnose and quantify structural heart disorders, and in particular valve stenosis and regurgitation and shunt lesions, Professor Baumgartner seized the opportunity, under the supervision of Professor Maurer, to study the Doppler assessment of prosthetic heart valves. Professor Baumgartner says, “Some key articles resulted from this work describing localised high velocities and pressure recovery as a source of major discrepancy between Doppler measurements and direct haemodynamic assessment. In a series of studies, we were able to clarify the marked differences between Doppler and invasive haemodynamic measurements of prosthetic heart valves. This work provided an important basis for the correct assessment of prosthetic valve function by Doppler and avoidance of the misdiagnosis of valve dysfunction.”

“A second important project focused on the assessment of myocardial viability by dobutamine echocardiography studying the relationship of echo findings with positron emission tomography and with histology in patients who eventually underwent transplantation.” This study demonstrated the potential of dobutamine echocardiography to predict functional recovery of myocardium because nuclear techniques detect smaller percentages of viable myocardium that may not suffice to improve ventricular performance after revascularisation.”

“These Were Pioneering Times in Adult Congenital Heart Disease and the First Time That It Was Recognised That Specialist Centres Were Needed”

In 1993, Professor Maurer was appointed chair of cardiology at the University of Vienna, and Professor Baumgartner joined him as associate professor of cardiology at the Department of Cardiology. “Fourteen special years followed,” Professor Baumgartner recalls. From developing a high-quality echo lab, including organisation, implementation of new techniques, and training of young colleagues, as well as building up a research group dedicated to cardiac ultrasound, the focus soon moved forwards to establishing a clinical and research programme of adult congenital and valvular heart disease.

“These were pioneering times in adult congenital heart disease and the first time that it was recognised that specialist centres were needed to provide appropriate care for this special patient group,” says Professor Baumgartner. “The remarkable improvement in the survival of patients with congenital heart disease led to increasing numbers of adult patients with congenital heart disease, in particular those with more complex disease. The wide variety of congenital defects and their specific long-term problems as well as the changing scope of problems due to the change in treatment policies and surgical/interventional techniques during childhood has remained a particular challenge for grown-up congenital heart disease care. It became clear that these patients have special needs and that the physicians taking care of them need particularly high experience that can only be developed in highly specialised superregional centres.”
Professor Baumgartner worked closely with Professor Maria Wimmer, MD, head of paediatric cardiology, Vienna General Hospital, to build up an adult congenital heart disease centre. Close collaboration with other centres in Europe and the United States was key to developing this programme. With the advent of catheter intervention in structural heart disease, interventional cardiology became a major new focus for Professor Baumgartner. Professor Peter Probst, MD, played a key role as a teacher in the development of a catheter interventional programme for structural heart disease. Combining a busy clinical programme with imaging and intervention in adult congenital and valvular heart disease provided a unique opportunity during the years in Vienna to set up a number of successful research projects.

In 2007, Professor Baumgartner moved to the University of Muenster, which had decided to establish an adult congenital heart disease centre. This was the common vision of Karla Voellm, who set up the EMAH Foundation to support adults with congenital heart disease, the head of cardiology, Professor Guenter Breithardt, MD, FESC, the hospital director Professor Norbert Roeder, MD, and the dean of the University, Volker Arolt, MD, who all helped to make it possible. The new Division of Adult Congenital and Valvular Heart Disease within the Department of Cardiovascular Medicine now provides comprehensive care for adults with congenital and valvular heart disease, Marfan’s syndrome, hypertrophic cardiomyopathy, and other structural heart disease. The service includes outpatient clinics, inpatient care, imaging, cardiopulmonary exercise testing, as well as catheter diagnostics and interventions for these patients. High-quality patient care is combined with research and education. Over the past 5 years, as director of the Division of Adult Congenital and Valvular Heart Disease, Professor Baumgartner has established “an excellent and ambitious team of people” to run a growing programme with 3500 outpatient visits, 750 inpatients, and 150 catheter interventions each year, a training programme in adult congenital and valvular heart disease, and successful research projects.

“A Number of Professor Baumgartner’s Group’s Articles Have Had an Impact on European Society of Cardiology Practice Guidelines”

Professor Baumgartner’s research focuses on clinical questions in the management of adult congenital and valvular heart disease. He says, “Development of excellence in adult congenital and valvular heart disease requires extensive clinical expertise. One needs to see patients, patients, and patients.” A number of his group’s articles have had an impact on European Society of Cardiology practice guidelines. They include an article on the outcome of asymptomatic severe aortic stenosis and the definition of a subgroup at increased risk by severity of valve calcification and haemodynamic progression rate,9 and a Circulation article in 2006 on the outcome of watchful waiting in asymptomatic severe mitral regurgitation, demonstrating that careful follow-up is safe in the absence of left ventricular dysfunction (size and ejection fraction), pulmonary hypertension, or atrial fibrillation.13 Professor Baumgartner adds, “Our studies on neurohormones as predictors of outcome in valvular and congenital heart disease demonstrated their potential role for the management of these patients and the timing of intervention. For asymptomatic severe aortic stenosis, our study was one of the key articles that led to the inclusion of marked brain natriuretic peptide elevation in the guidelines as a criterion for elective surgery.”11–13

Another study on atrial septal defect closure in adults demonstrated that even elderly patients benefit and can be safely treated by catheter intervention.14 Professor Baumgartner comments, “The negative impact on postinterventional outcome of pulmonary hypertension, which increases with age, highlighted that atrial septal defect closure should be performed, even at an advanced age, in asymptomatic or mildly symptomatic patients as soon as it is diagnosed.” Meanwhile, his group’s research into the long-term outcome of patients with small ventricular septal defects demonstrated that conservative follow-up is safe in adults if patients are asymptomatic, have normal pulmonary artery pressure, and show no signs of left ventricular volume overload.
Professor Baumgartner was chair of the European Society of Cardiology’s Working Group on Adult Congenital Heart Disease from 2006 to 2008 and has served on a number of other committees (practice guidelines, education, and congress programme). His major achievements include the guidelines on the management of grown-up congenital heart disease, for which he chaired the taskforce, and the first, and updated, guidelines on the management of valvular heart disease. In addition to funding from the Austrian Research Foundation, Professor Baumgartner’s work in Muenster in recent years has been supported particularly by the EMAH-Stiftung Karla Voellm (Adult Congenital Heart Foundation).

The Division of Adult Congenital and Valvular Heart Disease has become firmly established over the past 5 years. Professor Baumgartner hopes that it can continue to “contribute to development of the field and provide excellent care to many patients, and offer relevant research, and solid training.” The future holds many opportunities. “On the diagnostic side, the development of refined noninvasive imaging techniques and biomarkers that provide advanced anatomical as well as functional assessment, guiding improved therapy and its optimal timing,” he explains. “On the therapeutic side, close collaboration of interventional cardiology and cardiac surgery will lead to innovative new concepts such as optimal preparation for future catheter intervention by initial surgical repair or hybrid procedures.”

References

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“The Main Impact of Our Studies Will Be to Find Better Risk Stratification Methods for Sudden Cardiac Death in Various Populations to Be Used in the Field of Future Personalised Medicine”

Professor Heikki V. Huikuri, MD, FACC, FESC, professor of cardiology, director, Institute of Clinical Medicine, and chief physician of cardiology, University of Oulu, and University Central Hospital, Oulu, Finland, received a Finnish Foundation for Cardiovascular Research scholar - ship of €180 000 for his clinical cardiology research group in 2012 for a project on sudden cardiac death in type 2 diabetes mellitus.

The foundation has provided funding for the group for 2 decades and currently provides ≈25 percent of the group’s total funding, contributing to 2 lines of research. One line is focussed on analysis, interpretation, and signal processing of the electrocardiogram (ECG) using a mobile clinic database to evaluate the risk for sudden arrhythmic death. Digital ECGs are also being collected from the Northern Finland birth cohort-66 to study the relative role of developmental factors from birth to adolescence and the genetic factors obtained from the genome-wide analyses in predicting abnormalities in the ECG in middle age. The second line involves collecting a consecutive series of sudden cardiac deaths in collaboration with the Forensic Medical Department at the University of Oulu. This started 10 years ago and will continue for a further 10 years. “We have observed some differences in genetic variants between the victims of sudden cardiac death and controls in international collaborative studies,” says Professor Huikuri. “These studies will continue using more sophisticated genetic analysis methods and collecting better defined phenotypes.”

Professor Huikuri’s group collaborates with the group of Professor Tapio Seppänen, PhD, professor of medical technology, Technical Faculty, University of Oulu, and with a group in the Verve Institution, Oulu, directed by Mikko Tulppo, PhD, associate professor of cardiovascular...
physiology. Their many international collaborators include Professor Robert Myerburg, MD, University of Miami, FL; Professor John Rioux, PhD, University of Montreal, Montreal, Canada; Dan Arking, PhD, associate professor, John Hopkins University, Baltimore, MD; and Professor Georg Schmidt, MD, University of Munich, Munich, Germany.

Together with the group from the Technical Faculty, Professor Huikuri’s group has developed analysis methods for 24-hour ECGs and tested their significance in risk stratification. Professor Huikuri says, “One of the major findings has been that altered fractal heart rate dynamics is associated with an increased risk of mortality in post-infarction patients.” A recent study of new risk modifiers using the standard 12-lead ECG from the mobile clinic population, including >10,000 middle-aged subjects from Finland studied 40 years ago, revealed that early repolarisation in the inferior leads predicts sudden arrhythmic death.

“Many of Our Results Can Be Applied Directly to Clinical Work. With Rapidly Growing Knowledge on the Nature of Inherited Cardiac Diseases, the Need for Specialised Diagnostics Is Constantly Increasing”

Dr Heliö in the lab. Photograph courtesy of Dr Heliö.

Tiina Maria Heliö, MD, PhD, FESC, consulting cardiologist, Helsinki University Central Hospital and Meilahti Hospital, Helsinki, has received several grants from the Finnish Foundation for Cardiovascular Research, first for her doctoral thesis and later to conduct clinical and genetic research concerning inherited cardiomyopathies. “The recent grants [including a grant of €67,800 in 2012] have provided the opportunity to start up my own group at Helsinki University Central Hospital,” says Dr Heliö. “The funding has been used to cover research expenses and the salaries of a research nurse and PhD students. In Finland, there are few, if any, clinical posts in cardiology that would allow time for research work. Thus, the grants have also bought me valuable time to concentrate on research.”

Dr Heliö’s doctoral thesis on the molecular genetics of apolipoprotein B-100, the lipid-carrying molecule of low-density lipoprotein particles, showed that, in contrast to many other European populations, the mutations of apolipoprotein B-100 were an uncommon cause of hypercholesterolemia in the Finnish population. Due to ancient isolation, the genetic background of several inherited diseases in Finland differs from many other European populations.

“To be able to better treat patients of Finnish origin, we need to investigate our own population, the genetic aetiology and the genotype/phenotype relationships typical of the Finns,” says Dr Heliö. The thesis was supervised by Professor Matti J. Tikkanen, MD, PhD, and Professor Aarno Palotie, MD, PhD, at the University of Helsinki.

“Because I was specialising in internal medicine, I did postdoc research in the lab of Professor Kimmo Kontula, MD, PhD, at the University of Helsinki, exploring the genetic background of inflammatory bowel disease and learning linkage and genome-wide search methodologies,” says Dr Heliö. “However, I could not resist the challenge of cardiology, and when I received a clinical fellowship in cardiology, I changed the research subject to inherited cardiomyopathies, as suggested by my mentor, Professor Markku S. Nieminen, PhD.”

For more than a decade, Dr Heliö’s main focus has been the molecular genetics of inherited cardiomyopathies in Finns. She has worked closely with collaborators from the University of Eastern Finland and Helsinki University Central Hospital, including Professor Johanna Kuusisto, MD, PhD, Satu Kärkkäinen, MD, PhD, Professor Keijo Pekkarinen, MD, PhD, Professor Markku Laakso, MD, PhD, Professor Kontula, and Maija Kaartinen, MD, PhD. She says, “As a result of these collaborative efforts, several cardiomyopathy-causing mutations of the lamin A/C gene have been found and genotype/phenotype correlations are being assessed.” More recently, Dr Heliö has established collaborations with the groups of Tero-Pekka Alastalo, MD, PhD, University of Helsinki; Pekka Taimen, PhD, University of Turku, Turku, Finland; and Jyrki Lötjönen, PhD, and Professor Matej Oresic, PhD, VTT Technical Research Centre of Finland, Espoo, Finland.

Dr Heliö adds, “Many of our results can be applied directly to clinical work. With rapidly growing knowledge on the nature of inherited cardiac diseases, the need for specialised diagnostics is constantly increasing.”

References

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