

Department of Pediatrics and Adolescent Medicine

Division of Pediatric Cardiology

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Research focus

- Cardiopulmonary exercise testing and the cardiopulmonary capacity of children
- Influence of elite level athletics on cardiac health
- Myocarditis and sport
- Sports in Fontan patients
- Risk stratification after cardiac surgery
- Pathophysiology of the Fontan circulation
- Congenital Cardiology Cloud
- Echocardiography
- Pathophysiology of congenital heart disease in a rat model
- Multimodality imaging
- Interventional therapy
- Pharmacological studies

Structure of the Division

Professorship: 1

Personnel: 79

- Doctors (of Medicine): 22
- Scientists: 2 (thereof funded externally): 2)
- Graduate students: 20

Clinical focus areas

- Interventional therapy of congenital heart defects in the catheter laboratory
- Surgical therapy of congenital heart defects in close cooperation with the Division of Pediatric Cardiac Surgery
- Intensive care after cardiac surgery
- Specialized ambulatory services: congestive heart failure, transplant, arrhythmias, sports, Fontan-patients

Research

In the Division of Pediatric Cardiology, patient research on treatment techniques and care structures is performed. A particular focus is on different modalities of cardiovascular imaging and pathophysiology in univentricular hearts after Fontan operations. In basic research there are two working groups on the pathophysiology of congenital heart defects in the small animal model and a material biobank on the molecular genetic causes of congenital heart defects.

Cardiopulmonary exercise testing and the

cardiopulmonary capacity of children

PI: Dr. Dr. I. Schöffl, Dr. K. Rottermann
Cardiopulmonary exercise testing in very young children and in children with limited cardiopulmonary capacity presents several challenges. The bicycle ergometry as well as the one performed on a treadmill have several limitations when testing children. In a study with 7 – 10 year-old healthy children we were able to implement a field test, using a mobile cardiopulmonary exercise testing device. The children were instructed to perform 4 steps of 2 minutes with increasing speed after each step. The test was conducted in a local park. This way the children were able to run according to their own capabilities. In comparison to a cardiopulmonary exercise test performed on a bicycle the children all reached maximal exertion while enjoying themselves.

In a second study we now want to transfer this protocol onto even younger children (4 – 6 year-olds). At the same time the test protocol is being used in a multicentre study design to develop normal values for children aged 4 – 8 years.

Influence of elite level athletics on cardiac health

PI: Dr. I. Schöffl
Sudden cardiac death is the leading medical cause of death in young athletes. Detailed knowledge about the sport specific, cardiac adaptations are necessary in order to evaluate the influence of sports performed at an elite level on the heart and in order to develop adequate measures to prevent sudden cardiac death. In a first study in which we investigated the Junior German National Team in climbing we were able to show that climbing at an elite level led to characteristic cardiac adaptations, comparable to those observed in elite athletes from contact sports. In a second study we want to investigate the influence of an extreme endurance sport on the heart. The athletes from the German nation team in ski mountaineering, cross country skating and biathlon will be investigated using echocardiography with standard measurements in combination with strain measurements and cardiopulmonary exercise testing.

Myocarditis and sport

PI: Dr. Dr. I. Schöffl, Dr. A. Weigelt
The most common cause for myocarditis is a viral infection of the heart muscle. In Germany myocarditis represents the most common cause for sudden cardiac death in young athletes. The correlation between viral infection and the development of a myocarditis has been shown in animal models but not in humans so far. It is believed that athletes have a higher risk of viral infections and as a consequence of catching viral myocarditis. However, the number of patients is so small that this is mere speculation at this point. After having had myocarditis a rest from physical activity depending on the severity of the disease is recommended by the ESC. The level of evidence for these recommendations however, is poor, due again to the small number of patients. Since 2013 all myocarditis patients from 25 centres across Germany and Austria have been gathered to gain a

better insight into this disease. In a common approach with this MYKKE registrar we have now developed a questionnaire eliciting the influence of physical activity on the occurrence of myocarditis, the recommendations given by the treating physicians, the compliance to these recommendations as well the outcome after 12 months. In a second, prospective, multicentre approach myocarditis patients are closely followed and monitored over a timeframe of 24 months and provided with clear instructions and training plans when returning to sport.

Sports in Fontan patients

PI: Dr. A. Weigelt, Dr. Dr. I. Schöffl
The cardiopulmonary fitness can be estimated using cardiopulmonary exercise testing. The main parameter is the VO_2 peak which also represents the best prognostic value with regards to mortality, transplantation, and liver failure. The VO_2 peak can be increased by physical activity. In a study, in which the VO_2 peak of Fontan patients was compared to their physical activity during childhood and adolescence using a questionnaire, we hope to prove the positive correlation between sports and VO_2 peak. This could imply an improvement of the most important prognostic value through physical activity. In further studies we plan to implement intervention studies in order to improve the cardiopulmonary fitness and thus the long-term survival of our Fontan patients.

Risk stratification after cardiac surgery

PI: Dr. M. Schöber, Dr. R. Zant
The aim of this study is to identify patients with a high risk of profound shock by defined clinical parameters. Once identified, a structured approach is initiated to provide optimal organoxygenation. We use urinary lactate measures, which to the best of our knowledge has not been evaluated as prognostic parameter in critically ill patients so far. However, this method may be superior to serum lactate measurements in this patient collective: Urinary lactate summarizes a greater time period and therefore may be superior by equalizing short, but clinically irrelevant peak values. This study is supported by the Johannes und Frieda Marohn-Stiftung.

Pathophysiology of the Fontan Circulation

PI: Prof. Dr. S. Dittrich, Dr. J. Moosmann
Patients with univentricular heart malformations require several successive cardiac operations resulting in Fontan circulation: the univentricular heart supplies the systemic circulation and pulmonary circulation remains passive. The pathophysiological changes of the Fontan circulation are the focus of our research: By near-infrared spectroscopy (NIRS) measurements, we demonstrated that Fontan patients, especially with PLE, have alterations in perfusion ratios with low regional oxygen saturation (rSO_2). Moreover, by molecular genetic miRNA analysis, we succeeded in identifying altered miRNA-controlled immunological pathways in Fontan patients with PLE. We were able to

demonstrate these immunological changes in terms of altered lymphocyte populations as well as changes in T-cell differentiation corresponding to chronic inflammation. In a large cross-sectional MRI-analysis, we have shown that pathological abdominal and thoracic lymphatic pattern are present in a relevant number of Fontan-patients and that pathologic lymphatic pattern are associated to clinical symptoms after Fontan operations. These observations support the hypothesis, that the lymphatic system may play a crucial role in the Fontan-physiology.

Congenital Cardiology Cloud

PI: Dr. U. Doll, Dr. K. Rottermann

As part of the governmental program "Bayern Innovativ" (PBN-MED-1609-0004) and funding by the Bavarian State ministry for economics and media, energy and technology, a tele-medical platform could be established, meshing inpatient treatment with long-term ambulatory care.

Better use of medical findings, improved documentation and treatment planning and a strong emphasis on patient's involvement determine the subjects of the intersectoral cloud used in this healthcare research project. Incoming tele-medical consultations and second opinion requests are used for sharing patient related data such as medical reports and echocardiographic or heart catheterization diagnostic imaging. In addition, performing of live tele-medical videoconferences with referring physicians takes place, in order to discuss these diagnostic findings. Clinical data of interest can be shared with our patients via a tele-medical cloud and patients can be supervised by videoconference in their familiar domestic surroundings.

Pathophysiology of congenital heart disease in a rat model

PI: Dr. M. Alkassar

We examine changes in the development of power inside single cardiac muscle cells and tissue in diseased rats. These results are used to optimize a simulation software specifically designed to depict impending cardiac insufficiency at an early stage. The simulation illustrates the power inside the cardiac muscle in four dimensions and shows critical areas.

Funding: Klaus Tschira Foundation

Multimodality imaging

PI: Dr. M. Alkassar

Three-dimensional display of anatomical structures was used for planning of therapy. We established new three-dimensional display options with echocardiography, CT, and MRI which help to develop a realistic idea of heart and vessels. The use of such a display in the field of pediatric cardiology is investigated in various studies. We were able to prove an enormous advantage of 3D-heart models in the context of catheterizations. A following study currently investigates the benefit of 3D-imaging regarding the compensation of respiration and heartbeat. Another study investigates the advantages of 3D-models in the pre-procedural planning of surgical operations. Therefore we project very real-looking three-dimensional images of the heart with the help of a virtual reality glasses (VR) into the room. For a tactile perception, we also create three-dimensional life-sized pressure of the heart of silicone. The Division of Pediatric Cardiology is one of the leading international centers for the establishment and further development of multimodal methods for the treatment of children with heart disease in Germany.

Interventional therapy

PI: Dr. T. Abu-Tair

To estimate risk and prognosis of patients, who underwent perior and balloonvalvuloplasty of critical pulmonary valve stenosis and pulmonary valve atresia in infancy between 1996 and 2014, morphologic, hemodynamic und procedural data have been collected in a multicentric study. These data have been evaluated regarding prognostic impact at time of pulmonary valve replacement, surgical manipulation at the RVOT or RVOT-Stenting. Despite these over decades established and successful performed procedure there is still a lack of data regarding mid- and long-term-outcome. In addition, other interventional procedures to preserve ventricular function will be evaluated regarding risk-factors and long-term-outcome.

Pharmacological studies

PI: Prof. Dr. S. Dittrich, Dr. Martin Schöber

We completed the study "Effect and Safety of Treatment with ACE inhibitor enalapril and beta-blocker metoprolol on the onset of Left Ventricular Dysfunction in Duchenne Muscular Dystrophy", a long-going multicentric investigator-initiated pharmacology study in children and adolescents. The use of anti-congestive drugs in patients with Duchenne muscular dystrophy has now been included in the guideline recommendations. Currently there is an ongoing Phase III study of pharmacotherapy in children: the panoramic study of Novartis for the use of a combination preparation LCZ696 (sacubitril / valsartan) for the treatment of heart failure

Teaching

The Division of Pediatric Cardiology takes part in the general teaching program of the Department of Pediatrics and Adolescent Medicine. Additionally, medical students are taught pediatric cardiology within an elective course on pediatrics. Furthermore, we offer the possibility to perform clinical electives in our Division. MD doctorates are supervised.

Selected publications

Dittrich S, Weise A, Cesnjevar R, et al. Association of Lymphatic Abnormalities with Early Complications after Fontan Operation. The Thoracic and cardiovascular surgeon. 2020

Herrmann H, Cabet E, Chevalier NR, et al. Dual Functional States of R406W-Desmin Assembly Complexes Cause Cardiomyopathy With Severe Intercalated Disc Derangement in Humans and in Knock-In Mice. Circulation 2020 Oct 7. doi: 10.1161/PMID: 33023321

van Walree ES, Dombrowsky G, Jansen IE, et al. Germline variants in HEY2 functional domains lead to congenital heart defects and thoracic aortic aneurysms. Genet Med. 2020 Aug 21.

Söder S, Wällisch W, Dittrich S, et al. Three-Dimensional Rotational Angiography during Catheterization of Congenital Heart Disease A ten Years' experience at a single center. Sci Rep. 2020; 10: 6973.

Schöffl I, Ehrlich B, Stanger S, et al. Exercise Field Testing in Children: A New Approach for Age-Appropriate Evaluation of Cardiopulmonary Function. Pediatr Cardiol 2020.

Knieling F, Rüffer A, Cesnjevar R, et al. Transfontanellar Contrast-Enhanced Ultrasound for Monitoring Brain Perfusion During Neonatal Heart Surgery. Circ Cardiovasc Imaging 2020 Mar;13(3):e010073. doi: 10.1161

Stegmann H, Bauerle T, Kienle K, et al. 4D cardiac magnetic resonance imaging, 4D and 2D transthoracic echocardiography: a comparison of in-vivo assessment of ventricular function in rats. Laboratory animals 2019; 53: 169-179

Schroer S, Fahlbusch FB, Munch F, et al. Multisite measurement of regional oxygen saturation in Fontan patients with and without protein-losing enteropathy at rest and during exercise. Pediatric research 2019; 85: 777-785

Roschl F, Purbojo A, Ruffer A, et al. Initial experience with cinematic rendering for the visualization of extracardiac anatomy in complex congenital heart defectsdagger. Interactive cardiovascular and thoracic surgery 2019; 28: 916-921

Dittrich S, Graf E, Trollmann R, et al. Effect and safety of treatment with ACE-inhibitor Enalapril and beta-blocker metoprolol on the onset of left ventricular dysfunction in Duchenne muscular dystrophy - a randomized, double-blind, placebo-controlled trial. Orphanet journal of rare diseases 2019; 14: 105