Spotlight: Kurt Huber, MD, FAHA, FACC, FESC

“In-Hospital Mortality From ST-Elevation Myocardial Infarction Was Reduced From 15% in 2002 to ≈5% in Allcomers, Including Patients in Shock in 2010”

Kurt Huber, professor and director of the 3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna, Austria, talks to Mark Nicholls.

The Vienna ST-elevation myocardial infarction (STEMI) network in which potential patients are triaged by physicians of the Vienna ambulance system, in close contact with open catheter labs, has resulted in a significant improvement in clinical outcomes, and one of the driving forces behind it is Kurt Huber, MD, FAHA, FACC, FESC, formerly of the Department of Cardiology, University of Vienna, Vienna, Austria, and, since 2002, director of the 3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, Vienna. One hospital (the university clinic) is on duty for 24 hours a day, 7 days a week, while 5 additional hospitals are on duty every day from 7 to 15 hours, and 1 of these is the second active catheter lab on duty during the night. Professor Huber says, “This ‘rotational’ system (for night duty) is an advantage because only the most experienced interventional cardiologists are on duty. In-hospital mortality from STEMI was reduced from 15% in 2002 to ≈5% in allcomers, including patients in shock in 2010.” He adds, “The Vienna STEMI network was the trigger to create networks throughout Austria with the help of the Ministry of Health.”

The success of the network, which Professor Huber says has been the most enjoyable and important work of his career because of the “implication of the importance of networks on a national and international basis,” has led to international recognition. He was invited to present data from the network at the American Heart Association Scientific Sessions in 2010 and at several European Society of Cardiology meetings. He was also invited to join the European Society of Cardiology taskforce to update the STEMI guidelines (published in 2008) and write articles about STEMI networks for a number of leading publications.

“Scientific Interests Triggered My Switch From the Department of Gastroenterology and Hepatology to the Department of Cardiology”

Professor Huber was born in Linz, Austria, in August 1955, and he graduated in medicine in 1979 from the University of Vienna Medical School. He was then mentored by the late Professor Bernd Binder, MD, PhD, of the Department of Vascular Biology at the University of Vienna, who taught him basic research techniques and advised him when he was writing his first scientific articles. Professor Huber says, “We worked on the plasmin activation system in disease, especially on the isolation and characterisation of t-PA (tissue plasminogen activator) and u-PA (urokinase-type plasminogen activator) and the role of PAI-1 (plasminogen activator inhibitor-1).” Thus, from 1979 onwards, Professor Huber’s scientific interest was in endogenous fibrinolysis, first its role in oncology, and later, in cardiovascular disease. That interest eventually led to a focus on cardiology.

In 1981, Professor Huber moved to Innsbruck University, Innsbruck, Austria, for his education in oncology, haemostaseology, and emergency medicine, but he
returned to Vienna in 1982 to the 2nd Department of Gastroenterology and Hepatology at the University of Vienna. After several articles in gastroenterology and oncology, he became more interested in cardiovascular disease. He explains, “Scientific interests triggered my switch from the Department of Gastroenterology and Hepatology to the Department of Cardiology, with Professor Fritz Kaindl, MD, and later, Professor Gerald Maurer, MD, FESC, FACC, where I stayed until 2002.” Both Professor Kaindl and Professor Maurer provided further mentoring, while Professor Otmar Pachinger, MD, FESC, FAHA (see http://circ.ahajournals.org/cgi/reprint/121/17/f97) taught him interventional cardiology.

From 1986, Professor Huber directed the basic science lab, worked on the wards and in outpatients, and was an active member of the interventional team at the University of Vienna. He qualified as a specialist in internal medicine in 1986, in cardiology in 1988, and in internal intensive care in 2002. He was appointed professor of internal medicine and cardiology at the University of Medicine in Vienna in 1995 and director of the 3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, in 2002.

Wilhelminen hospital is an academic hospital, working closely with the Medical University of Vienna in educating students and on scientific projects. The department has 81 beds, including 10 emergency care and 9 intensive care beds, with 39 physicians including 10 cardiologists and 4 intensive care specialists. In 2010, the hospital cared for 35000 emergencies in internal medicine (emergency division), and 3500 patients were treated in 2 cardiology wards. A further 13000 patients were seen on the outpatient ward, which specialises in treating postcoronary intervention patients, patients with rhythm disorders, and those with chronic heart conditions as well as valvular and structural heart disease.

Professor Huber says, “We offer all conservative and interventional diagnostic and therapeutic methods in cardiology, including percutaneous coronary intervention, stenting, pacemakers, implantable cardiac defibrillators, ablation of rhythm disturbances, occlusion of septal defects, and transfemoral aortic valve replacement.” He also teaches interventional cardiology to students at the Medical University of Vienna, leads the practical training for students at his institution, and oversees his own 8-strong study team of postdoctorates, which is involved in international trials.

Professor Huber is very happy with his current role, and says, “My position as director of the 3rd Medical Department is optimal with respect to responsible clinical work, including coronary interventions, organisation of a huge department, education of young physicians in clinical and scientific work, organisation of academic studies, and participation in international trials.”

“The Main Target of the Research Is to Reduce the Burden of Acute Coronary Syndromes”

Professor Huber’s major research interests include the pathophysiology, diagnosis, and treatment of acute coronary syndromes; the mechanisms of restenosis and stent thrombosis; the plasmin activation system in disease; thrombolytic, antithrombin, and antiplatelet therapy; inhibitors of the renin-angiotensin system; and diabetes mellitus in heart patients. He says, “The main target of the research is to reduce the burden of acute coronary syndromes.”

Research that has been particularly enjoyable includes his work on the management of acute myocardial infarction in patients presenting with persistent ST-segment elevation and with the Task Force on Myocardial Revascularisation of the European Society of Cardiology.

Other important research includes studies of the prehospital use of glycoprotein IIb/IIIa-blockers in the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX AMI) trial; antithrombotic management of atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing coronary stenting; prehospital reperfusion therapy, and enhancing the efficacy of delivering reperfusion therapy, respectively.

Since 2000, Professor Huber has enjoyed working on permanent research projects with his “inspirational” friend Professor Johann Wojtu, PhD, of the Department of Cardiology, Medical University of Vienna. His key scientific mentors are Professor Allan Ross, MD, George Washington University School of Medicine, St. Petersburg, FL, Professor Bernard Gersh, MD, FRCP, Mayo Clinic College of Medicine, Rochester, MN, and Professor Freek Verheugt, MD, chair, Department of Cardiology, Onze Lieve Vrouwe Gasthuis, Amsterdam, the Netherlands (see http://circ.ahajournals.org/cgi/reprint/118/9/f49). Professor Huber is involved in a number of international trials, in most cases as a steering committee member and national coordinator for Austria. He has published >300 peer-reviewed articles to date.

Aiming to “Stay Healthy and Be Involved in High-Quality Work for as Long as Possible”

Professor Huber’s clinical work is funded by the Vienna Hospital Association, and his scientific work is financed by the Austrian Association for the Promotion of Research in Arteriosclerosis, Thrombosis, and Vascular Biology (ATVB); the Ludwig Boltzmann Association; and national and international grants for certain academic studies. The ATVB was founded in 2000, and from its inception, he has been a director of the organisation. In 2002, Professor Huber became director of the Ludwig Boltzmann Institute for Interventional Cardiology and Rhythmology in Vienna, which is part of the Cluster for Cardiovascular Research at the Ludwig Boltzmann Association.

For the past 16 years, Professor Huber has been a board member of the Austrian Society of Cardiology, and was secretary general from 1999 to 2006, president elect from 2006 to 2007, and president from 2007 to 2009. He was a member of the Committee for European Union Relations of the European Society of Cardiology from 2002 to 2004, and since 2005 he has been a permanent member of the European Society of Cardiology Press Committee, which
he has coordinated since 2010. He is a permanent board member of the Working Group on Thrombosis of the European Society of Cardiology, and was president from 2006 to 2008. He is also a board member of the European Society of Cardiology’s Working Group on Acute Cardiac Care.

Professor Huber believes interventional cardiologists will increasingly focus on techniques that will reduce the need for cardiac surgery. He says, “I see a bright future for cardiology, which will take over present indications for cardiac surgery based on better interventional techniques that are currently approved, for example, transcatheter aortic valve implantation, reopening of chronic coronary occlusions, multivessel interventions, and many more. The development of more efficacious and safer antithrombotic agents is one of the most interesting fields nowadays in cardiology.” He adds, “At the same time, we will have to deal with elderly patients and chronic states of diseases, and it will be a challenge to implement and adapt the existing guidelines for this increasing group of patients.” His own future goals are to “stay healthy and be involved in high-quality work for as long as possible.”

Selected References


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Research carried out by Linda W. van Laake, MD, PhD, a cardiology resident at University Medical Center Utrecht, Utrecht, the Netherlands, has included transplanting human embryonic stem cell-derived cardiomyocytes into the infarcted heart. She says, “At the time, we were not able to select cardiomyocytes only. It was a mixture of cells, and we found that only cardiomyocytes survive a transplantation in the infarcted heart.”1 This research resulted in Dr van Laake’s first main article from her PhD, which she worked on between 2004 and 2007 at the Heart Lung Center Utrecht and the Hubrecht Institute in Utrecht, supervised by Professor Pieter Doevendans, MD, and Professor Christine Mummery, MD, PhD.

The transplanted cells improved cardiac function, but in the short term, after 4 weeks, the cardiomyocytes improved function more than the other transplanted cells. Dr van Laake then looked at long-term cardiac function and found that, after 3 months, the cells did equally well.2 It meant that, in the long term, it was not necessary to transplant cardiomyocytes; the improvement could be achieved with any cell type. Until then it had been thought that transplanted cardiomyocytes actively contributed to cardiac contraction, but now it seemed that a paracrine effect was more important. Dr van Laake says, “In a way it was a disappointment, because everybody hoped that it would be a true muscular effect, but it was good to realise what we were looking at and how we should proceed to improve things. Before that time, the impression in the field was that it was going to be very easy—we inject some cells and then we are there.” Scientists were keen to take the cells to clinical trials, but this article showed that it was too soon.

In the follow-up article, Dr van Laake looked at whether increased graft size, achieved by injecting more cells, would give better results. Surprisingly, functional improvement was less with large grafts, a result they still do not fully understand and are continuing to investigate.3 Dr van Laake says, “It showed again that even though the cell transplantations improved cardiac function, it was not as simple as just using large grafts. It was not the graft size: it was how much the cells were able to stimulate vascularisation. That is now quite a common way to think about this.” The transplanted cells also prevented apoptosis of the host cardiomyocytes by excreting cardioprotective factors and, potentially, factors that stimulated endogenous stem cells.

The researchers also found fibrosis and extracellular matrix around the grafts of human to mouse transplants and realised that it was important to conduct studies in larger animals to see whether that resulted in less extracellular matrix formation.

Dr van Laake’s Genetic Screen Revealed Similarity in Genome-Wide mRNA Expression in Induced Pluripotent and Embryonic Stem Cells

To continue her work, Dr van Laake then went to the lab of Deepak Srivastava, MD, director of the Gladstone Institute of Cardiovascular Disease, University of California, San Francisco, CA, who supervised her postdoctoral fellowship from December 2007 to January 2009. During that time, Dr van Laake was supported by an Interuniversity Cardiology Institute of the Netherlands fellowship and studied induced pluripotent stem (iPS) cells and micro-RNAs. One advantage of iPS cells over embryonic stem cells is that they can be derived autologously, circumventing ethical and immunological issues. It was a new area. Induced pluripotent stem cells were first described in 2006, and human iPS cells were described in 2007.

Researchers had already derived cardiomyocytes from iPS cells and looked at some surface markers and proteins, but nobody had done a real genetic screen, so that is what Dr van Laake did. She differentiated iPS cells and embryonic stem cells to cardiac progenitors. Expression of NKX2-5, an early cardiac transcription factor, was marked by a transgenic green fluorescent protein, so Dr van Laake could select and investigate cardiac progenitors rather than a whole mixture of cells. A genetic screen revealed unexpectedly high similarity in genome-wide mRNA expression levels.4 Dr van Laake explains, “That was a great finding, because it tells you that you can actively pursue iPS cell differentiation and transplantation, but it would also be very useful for drug screening.”

Like Maastricht University, Maastricht, the Netherlands, and the Hubrecht Institute, the Gladstone Institute was a work-hard, play-hard atmosphere, and Dr van Laake loved it. It was an inspiring place, with plenty of facilities, good guidance, and an abundance of training and resources. Professor Srivastava, “a very bright, positive person,” gave her complete freedom to decide what she wanted to investigate and then facilitated the work and gave guidance.
“Anything is possible,” says Dr van Laake. “That’s really great, especially when you are at the postdoc level. You want to follow your own path, and he really lets you do that.” Dr van Laake’s work on micro-RNAs in San Francisco has yet to be published, but she already has a publication in the field, a Circulation article from 2007, in which she collaborated with Thomas Thum, MD, PhD, from the University of Würzburg, Würzburg, Germany.5 She recalls how she met Dr Thum’s group at a conference: “We were just talking science. You know how that goes, at a conference it is really great to interact and get new ideas from each other.”

Dr Thum was investigating micro-RNAs in adult human failing hearts and Dr van Laake had access to fetal hearts because of her work on cardiac progenitor cells. She suggested that they do the same screen in the fetal heart to see whether there was a comparable upregulation of fetal genes and fetal micro-RNAs in the failing heart. It was known that in failing hearts there was upregulation of the fetal gene programme, and this would provide confirmation on a micro-RNA level. The hypothesis was correct, and has formed the basis of Dr Thum’s ongoing work on micro-RNAs in failing hearts. Dr van Laake has been investigating micro-RNAs in apoptosis and myocardial infarction with Li Qian, PhD, of the Gladstone Institute.

Dr van Laake’s work with fetal hearts stemmed from another successful collaboration on cardiac progenitor cells. Cardiac progenitor cells were isolated from fetal hearts and adult human hearts and differentiated in vitro or transplanted directly into an infarcted mouse myocardium. Both the undifferentiated cardiac progenitor cells and the differentiated progenitor cells preserved long-term function of the heart after myocardial infarction.6 The collaboration was with Professor Marie-Jose Goumans, PhD, at Leiden University Medical Centre, Leiden, the Netherlands. Both groups used the same mouse model and the same surgery and then conducted identical analysis and follow-up of function. The results were very comparable. Dr van Laake says, “I think people should collaborate more and exchange their cells, undifferentiated and differentiated, and use the same models so we can really compare what would be the ideal cell type for regeneration.”

**Awarded the Einthoven Dissertatieprijs in 2009 for the Best PhD Thesis in Cardiology in 2008**

Dr van Laake’s first research experience was at Maastricht University, where she studied medicine from 1998 to 2004. Her interest in cardiology was subconsciously influenced by her exposure to several family members with cardiac disease. At first she wanted to be a vascular surgeon, but eventually she decided on cardiology.

Dr van Laake was introduced to research by Tryfon Vainas, MD, a clinician and a PhD student at the time who is now working as a vascular surgeon in London, England, where he had gone for an internship. He helped Dr van Laake secure the same vascular surgery internship towards the end of her medical degree at Charing Cross Hospital, Imperial College, London. It was also her first rotation abroad in research. She worked in the vascular surgical department and helped with the Endovascular Aneurysm Repair Trial run by Professor Roger Greenhalgh, MD. The trial was comparing open and endovascular aneurysm
Also funded her undergraduate research and some travel grants during that period. The Netherlands Heart Foundation has also awarded her several travel grants.

As for her own research, Dr van Laake thinks the development of iPS cells is a great addition to the field and will really change things, especially in drug research. She says, “You can have the perfect patient model because you can take iPS cells from patients, differentiate them, and find out the effects of drugs.” In transplantation, she believes the way forward for regeneration will be tissue engineering instead of just injecting cells, although the latter may be useful for paracrine effects. “Another increasing realisation,” she adds, “should be that we do not only want cardiomyocytes to be in there but to have a real tissue that gets vascularised and can be self-supporting in the way that it connects to the host tissue.”

### References


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