A short phrase in a clinical paper illustrates that Croatian cardiologists have in the recent past faced clinical research obstacles that few of their medical colleagues in more fortunate environments elsewhere in Europe are likely to encounter. A review of a large series of patients with cardiac myxoma, who were seen between 1975 and 1994, comments that “we could not evaluate all the patients long enough because of some paramedical circumstances.” The “paramedical circumstances” were the long period of civil unrest and war and the subsequent migrations in the 5 years of conflict that followed Croatia’s independence from the then Yugoslavia in 1991.

Dr Davor Milicic is professor of medicine and cardiology and chief of the intensive cardiac care and the heart transplant programme at the University Hospital Centre, Zagreb, one of the authors of the paper on cardiac myxoma, and now president of the Croatian Cardiac Society. He said that although Croatian hospitals were heavily bombed and some were destroyed by the Yugoslav army and Serbian paramilitary troops during their war with Croatia in the 1990s, the health system on the whole continued to function well during the war. This was due to good organisation by the Croatian Ministry of Health and the enthusiasm of doctors and medical staff. “If we compare the health services with some other parts of the public infrastructure in Croatia, they did the best,” he says.

When peace came, cardiologists relished the opportunity to develop their specialty. In the 10 years of relative peace that have followed the end of the war, Croatia has rebuilt a health system infrastructure. Dr Milicic considers the crude statistics from recent data encouraging, even though mortality and morbidity indicators are still worse than the European Union average. In cardiology, waiting times for invasive procedures or elective percutaneous coronary intervention (PCI) are usually no longer than 2 to 3 months, and for coronary artery bypass grafts, the wait is about 4 months. “Not so bad,” comments the professor.

There are currently about 9 cardiologists per 100 000 inhabitants, a ratio that is similar to the United Kingdom. However, Dr Milicic believes that maintaining those levels may prove difficult. “There is an underproduction of young doctors in Croatia, and we will soon not have enough specialists to replace all the doctors who retire.”

Croatia’s health system suffers from the same limited resources that afflict many European countries, and the patients are traditionally used to unrestricted and free access to all kinds of medical help. There are policies to contain costs and to bring about greater financial stability to the system. “We have problems of a financial nature that mean, for example, that we do not implant enough drug-eluting stents. Only 1% to 2% of patients who have a PCI have one.” And the number of automatic cardioverter defibrillators used is less than Dr Milicic would like to see.

He is concerned that despite good intentions, further financial pressures would mean it would prove impossible to cover the growing medical needs of the population. “I would like to see a situation where we can follow most advances in cardiac care, whether it is pharmacotherapy or cardiac intervention.”

About 360 members of the Croatian Cardiac Society (CCS) have been making their own contribution to the improved health of their population, with initiatives such as the Croatian
Cardiovascular League, the Association for the Healthy Heart, national registers and guidelines, telecardiology for remote areas and the Croatian islands, and the development of an emergency PCI network, supported by the Ministry of Health. There is much pride in this network that already ensures efficient emergency PCI for half the Croatian population, and it is still expanding.

The CCS has been recognised as a leader in making people aware of the impact of cardiovascular disease, harmonising subspecialities, and introducing a quality of cardiac care that follows the policy and guidelines of the European Society of Cardiology (ESC). The CCS, together with the 14th Alpe Adria Cardiology Congress, is organising the 1st International Cardiology (ESC). The CCS, together with the 14th Alpe Adria Cardiology Congress, is organising the 1st International Cardiology Congress of the Croatian Cardiac Society in Dubrovnik, from 3-7 May 2006. The meeting will be conducted in English, and it is expected that many participants will come from abroad, including the president of the ESC, and a number of world experts in various fields of cardiology.

But when he is asked about his biggest hope for Croatian cardiology, Dr Milicic looks not only to the development of better services, or the introduction of sophisticated technologies, but to a new generation of internationally recognised cardiologists. “I would like to see many more young cardiologists trained,” he said, “because we really need them.”

Mark Pownall is a freelance medical writer.

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**Focus on Facts: Acute Stenting for STEMI**

The rates of primary percutaneous intervention for ST-elevation myocardial infarction (STEMI) vary widely throughout Europe. Deanna Wilson, BA, investigates some of the reasons.

The last 25 years have seen a notable rise in the use of percutaneous coronary intervention (PCI) by cardiologists all over Europe, and there is a general consensus that angioplasty in acute myocardial infarction (AMI) produces better outcomes than thrombolysis.

Yet the rate of PCIs per angiogram varies from over 50% in France to just over 20% in Latvia (Figure 1). Although not all angiograms are performed because there has been an AMI — meaning that the figures may not be wholly comparable — this wide range in the ratio of PCI to AMI strongly suggests that some countries are more active than others in implementing PCI in AMI patients. The reasons boil down to logistics and the available infrastructure.

Where prehospital care in AMI is concerned, the crux of the matter is to get the patient to an appropriate hospital. In France, the Service d’Aide Médicale d’Urgence (SAMU) acts as a central emergency point. It triages all emergency cases and organises rapid responses. If AMI is suspected, a medical intensive care unit team is dispatched to confirm AMI and initiate treatment.

It may be no surprise to find France topping the chart, but Slovenia in second place is perhaps rather surprising. According to Danny Schoors, MD, professor of cardiology at the Department of Cardiology, Laarbeeklaan, Brussels, Belgium, the reason stems from a period in 1991 following Slovenia’s 10-day war that resulted in the country’s liberation from what was then known as Yugoslavia, after which the government put its helicopters and pilots to a new health-orientated use. Today they carry some 98% of patients with AMI to hospital.

Holland is another well-organised country, says Dr Schoors. “It has 18 catheter laboratories and good networks of communication between the hospitals. ECGs can be taken at home, and patients taken immediately to hospital. In Belgium, the ambulance service is not so well organised, although a doctor and nurse will go out with the ambulance if a patient has chest pain.” Dr Schoors continued, “Also, some Belgian hospitals do not do PCIs. Although Holland’s service is better, it costs 20 times more than Belgium’s.”

In many European countries, the trends in annual PCI use are rising (Figure 2). But they did not all start from the same baseline, a factor that was particularly marked in the United Kingdom. Whereas the angioplasty rate for AMI

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**Figure 1.** Percentage of PCIs per angiogram shown for each European country (2003).

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**Figure 2.** for Working Group on Interventional Cardiology (WG 10) of the ESC. *EuroIntervent J.* In Press.
Developments in Cardiology  
Research in Scotland

Scotland has a high level of cardiovascular disease, but, according to Judy Ozkan, BA, research is under way to alleviate the situation.

Scotland has world-famous medical schools and a high percentage of life science graduates who provide a large skills base, and the country is well positioned for clinical research and drug development. Five Scottish universities — 3 of which have a top rating in the UK’s Research Assessment Exercise — are currently active in cardiovascular research. This is strategically important in a country trying to shake off a reputation for being the “sick man of Europe.”

Amongst Scotland’s population of just under 5 million, the death rate from coronary heart disease (CHD) is 244 per 100 000 for men and 90 per 100 000 for women. The UK average is 181 per 100 000 for men and 65 per 100 000 for women. In the more affluent southeast of England, this figure drops to 151 per 100 000 and 46 per 100 000 respectively. Glasgow, which is set to become a world-class centre for drug development and clinical research through a recent public sector-backed initiative, has the worst record of all, with rates exceeding 290 per 100 000, despite its achievements in clinical innovation.

Genetic Markers for Hypertension

An important strand of pioneering research that started in the 1960s in Glasgow and continues to this day involves hypertension. The work of Tony Lever, FRCP, former director of the UK’s Medical Research Council (MRC) Blood Pressure Unit at the University of Glasgow, is continued by the British Heart Foundation Blood Pressure Group, under the leadership of Anna Dominiczak, FRCP, of the Department of Medicine and Therapeutics and Head of the Division of Laboratory Research at Glasgow University.

Dr Dominiczak, along with John Connell, FRCP, (the current head of the MRC Blood Pressure Group), is leading a British and European studies of genetic markers in rodent models and humans for human essential hypertension. Funding is from the MRC’s UK-Bright Study and the European network to develop genetic markers for essential hypertension (EURNETGEN). The studies are based on a genome scan strategy that will ultimately lead to positional cloning of genes responsible for susceptibility to or severity of hypertension, left ventricular hypertrophy, and sensitivity to brain ischaemia in the stroke-prone spontaneously hypertensive rat. The team hopes to directly transfer these discoveries to essential hypertension in humans.

Primary Coronary Prevention

The West of Scotland has also been the focus of large cardiovascular investigations into primary coronary prevention. The West of Scotland Coronary Prevention Study (WOSCOPS), led by James Shepherd, FRCP, director, and Stuart Cobbe, FRCP, coprincipal investigator (both of the University of Glasgow), was a landmark primary prevention trial of the drug pravastatin in 6000 middle-aged men.

The study showed, for the first time, the benefits of a lipid-lowering drug in reducing the risk of heart attack in established and nonestablished cases of heart disease, coronary mortality and deaths from any cause. This research has been extended in the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) study, focusing on reducing the incidence of coronary episodes with pravastatin in the elderly population.
The MIDSPAN Study
Glasgow and the surrounding area provide the setting for one of Scotland’s largest and longest-running studies into cardiovascular disease. MIDSPAN (so called because it spans the middle age years) is now in its 30th year, and is a series of occupation and general population health studies looking at intergenerational trends in heart and lung disease and cancer.

Over 23 000 people have been involved in MIDSPAN at some time. It was pioneered by Victor Hawthorne, FRCP, a Scot who began his career in Glasgow and is now emeritus professor of epidemiology at the University of Michigan in Ann Arbor. Unusually for studies carried out in the 1960s and 1970s, all the study populations included women, and in 1 study over 4000 married couples were included. This paved the way for a later study called the MIDSPAN Family Study, carried out in 1996, involving 1040 sons and 1298 daughters aged 30-59 from 1477 families.

The high response rate to MIDSPAN means the findings are reasonably representative of populations living and working in areas characterised by high rates of socioeconomic deprivation and early mortality. Most of the investigations, which have been carried out using the MIDSPAN data sets, have involved epidemiological analyses of cross-sectional and longitudinal data, making use of the unusually rich combination of baseline and outcome variables.

A range of secondary studies has also been carried out, using the original survey data as a sampling frame, and incorporating a variety of research methods, both qualitative and quantitative, to study subgroups of interest. A feature of many studies has been collaboration between researchers from different institutions with different professional backgrounds and research disciplines. MIDSPAN is centred at the University of Glasgow, and is currently overseen by Graham Watt, FRCGP, professor of general practice at Glasgow University and chair of the MIDSPAN Steering Committee.

Long-Distance Analysis of ECGs
Instrumental to the WOSCOPS, PROSPER, and The British Regional Heart Study has been the development of computer software for long-distance analysis of electrocardiograms (ECGs) by Peter McFarlane, FRCP, professor of electrocardiology at the Department of Cardiology and Exercise Medicine at Glasgow Royal Infirmary. This work provided interesting electrocardiographic observations in relation to risk factors for ischaemic heart disease. Dr McFarlane currently directs an ECG core laboratory based at the Glasgow Royal Infirmary, which handles ECGs recorded in national and international clinical trials and epidemiological studies. The group has an extensive commercial collaboration with Spacelabs Burdick and Siemens of Deerfield, WI, in the United States, who are worldwide marketers of the Glasgow ECG analysis program.

Heart Failure Research
Another Glasgow-based project, the Heart Failure Research Group, is run by John J.V. McMurray, FRCP, professor of medical cardiology and honorary consultant cardiologist at the Western Infirmary. This focuses on the epidemiology, vascular pathophysiology, clinical pharmacology, clinical trials, and multidisciplinary management of chronic heart failure. One interest is reducing morbidity and mortality by attenuating vasoconstrictor pathways (such as the renin-angiotensin system and the sympathetic nervous system) and vasodilator pathways. Dr McMurray is cochair of the Valsartan In Acute Myocardial Infarction Trial (VALIANT), a long-term study conducted on survivors of heart attacks with the angiotensin II receptor antagonist valsartan, which has been shown to reduce death and prevent recurrent heart attacks in patients as effectively as standard angiotensin-converting enzyme inhibitor treatment. This offers physicians another therapeutic option for their patients.

Future Plans
The Scottish Executive (the devolved government for Scotland) plans to use Glasgow’s clinical expertise to benefit the local economy and ultimately overcome the city’s poor health. In April 2005, Minister Andy Kerr launched a £12.8 million project to promote Glasgow as the lead European centre for research and clinical trials with an emphasis on cardiovascular disease. The Glasgow Biomedicine project, a collaboration between the National Health Service in Greater Glasgow and Glasgow University, aims to give the population access to revolutionary treatments and to attract major pharmaceutical and biotechnology companies to Scotland. It will provide the infrastructure for a major expansion of clinical research in Scotland.

References

The opinions expressed in Circulation: European Perspectives in Cardiology are not necessarily those of the editors or of the American Heart Association.

Editor: Thomas F. Lüscher, MD, FRCP, FACC
Managing Editor: Keith Barnard, MB, BS, MRCS, LRCP
We welcome your comments. E-mail the managing editor at kbarnard@lww.co.uk