Chronic kidney disease is now considered more often as an important risk marker for cardiovascular disease than as a predictor of progressive kidney failure. Until recently, however, the link between kidney disease and cardiovascular risk was largely unrecognised.

One of the first researchers to put forward the theory that the kidney should be considered part of the cardiovascular system and that treatments for hypertension could also significantly reduce target organ damage was Dr Luis Miguel Ruilope, head of the hypertension unit at the 12 de Octubre Hospital in Madrid, Spain, associate professor of internal medicine at the Computense University, and president of the Spanish Hypertension Society.

“I have always insisted that there is a relationship between renal function and cardiovascular risk, which now is a well-accepted belief. But when I published some reviews in the 1990s defending the hypothesis that renal function and cardiovascular risk were related, at that time nobody paid attention,” he says. “Later on, of course, it was proven that this link was extremely important.”

Dr Ruilope trained in medicine at the University of Madrid and did his residency at the Clínica Jiménez Díaz, also in Madrid. He specialised in nephrology and took a position in the department of nephrology at the 12 de Octubre Hospital (see Figure), where he continues to work. In the late 1980s, Dr Ruilope decided to expand his clinical and research interests to include hypertension as well as nephrology, and he set up a hypertension unit in the hospital in 1987. As he explains, his reasons for doing so were pragmatic as well as academic.

“I knew about the relevance of arterial hypertension to nephrology and that arterial hypertension is a very prevalent disease,” he says. “It seemed to me that hypertension offered scope for doing research funded by private companies, including the pharmaceutical industry, as well as by the administration.”

The research that Dr Ruilope does in his clinic has always been heavily influenced by his involvement with scientists working on more basic scientific problems. His collaboration with Juan Carlos Romero, MD, who was then working at the Department of Physiology And Hypertension at the Mayo Clinic in Rochester, Minn, and with whom he worked between 1981 and 1989, was particularly fruitful. This led to his first study on the impact of antihypertensive medicine on the progression of renal failure. “The Mayo Clinic researchers were working in preclinical investigation, looking at different animal models of hypertension and the relationship between hypertension and the kidney. By collaborating...
with them, I got some interesting ideas,” he recalls. One of the ideas put forward by the Mayo Clinic that he decided to put to the test was the theory that angiotensin-converting enzyme inhibition could slow the progression of renal failure in patients with hypertension. The theory had been demonstrated in animal models but not in humans. Dr Ruilope tested the theory on a small group of patients with chronic renal failure whose hypertension was being treated with diuretics. He showed that switching them to captopril, an angiotensin-converting enzyme inhibitor, for a period of 12 months led to a significant slowing in the progression of renal failure.

“This proved that by using an angiotensin-converting enzyme inhibitor, you could change the evolution of renal failure. The trend and velocity of decay in renal function were really slowed in this group of patients. I feel really proud of this research,” he says.

Since 1990, he has worked in collaboration with the Department of Physiology at the University of Madrid, and he continues to believe that collaboration with preclinical researchers is important for anyone doing clinical investigations. Dr Ruilope has always considered research to be an important part of his hospital work, and he believes that, wherever possible, they should go hand in hand.

“Clinical research should, in my opinion, be a part of clinical practice in the hospital. If you are able to set up a clinical unit like the one I have, then you can gather information from your daily practice, and when you come across questions for investigation, you can try to integrate as many as possible into that clinical practice. That way, you improve your practice through research.”

However, Dr Ruilope’s current main interest is a project taking place outside of the hospital, in primary care. Collaborating with a number of other hypertension centres in Madrid and Barcelona, Spain, and the Carlos III Institute of Public Health in Madrid, he has set up a large study including a network of doctors in primary care medicine and has provided them with ambulatory blood pressure–monitoring devices and educational tools.

The project is designed to see how well hypertension and other cardiovascular risk factors are being controlled in primary care in Spain. Dr Ruilope believes that the study’s findings will surprise many specialists who believe that primary care medicine is not doing a good enough job.

“The truth is that the early detection of risk and of target organ damage as a consequence of cardiovascular disease in the early stages is really good in primary care medicine,” he says. The first paper showing results from the project was recently published in the journal Hypertension.

References


Spain is a world leader in harvesting organs for transplantation. Rafael Matesanz, MD, director of the Organización Nacional de Trasplantes in Spain, talks to Mark Nicholls about what lies behind this success and how other countries are following the model.

Heart transplantation programmes in many countries are limited because of a shortage of donor organs, and this is a matter of great concern. Yet Spain seems to be bucking the trend, successfully increasing the number of donor hearts and other organs that are made available through an innovative national programme.

Not only has the Organización Nacional de Trasplantes (ONT) in Spain been successful in procuring organs, but that success has been sustained since the body was first established in 1989. For cardiac surgeons, it means that hearts are more readily available; for patients, it means a reduced waiting time for transplantation surgery.

The ONT works closely with heart surgeons on the donor programme. Dr Rafael Matesanz, director of the ONT, says, “All technical decisions about patient priority and heart allocation are discussed and adopted in close cooperation with cardiologists and heart surgeons. The results are reviewed periodically and adapted to any new circumstances.”

As a result of the programme, waiting times and waiting lists in Spain have decreased during the last few years. For example, in a country with a population of 44 million, heart transplantation waiting lists fell from 116 patients in 2004 to 85 patients in 2005, a reduction of 26.7%. Waiting times fell from 74 to 63 days during the same period, with a mortality rate for patients on waiting lists of 6.4%.

Dr Matesanz, who developed the ONT system, says, “Spain is the only country with a sustained increase of organ donation during the last 17 years.” There has been a rise from 550 to 1546 annual donors and from 14.3 to 35.1 donors per million of the population. This is for all organs, not just hearts. “It is not an episodic increase, and some of the Spanish regions are even over 40 donors per million. So, it is a very strong and consolidated system,” he adds.

Comparable figures (Figure 1) show that the United Kingdom has 12.8 organ donors per million of the population; Germany, 14.8; Italy, 21; France, 22.2; and Austria, 24.8. In the United States, the rate is 25.5 per million. Figures for heart transplantations show that Spain carries out 6.5 operations per million of the population; the United Kingdom, only 2.6; France, 5.8; Italy, 6.0; Austria, 6.9; and the United States, 4.7. In 2005, Spain carried out 287 heart transplantations—about 6% of all heart transplantations in the world.

It is hardly surprising that a number of other countries are now following the Spanish model, with increasing success. Dr Matesanz explains, “The best adaptation is in Tuscany in northern Italy, which is expected to reach a figure of 40 donors per million for 2006.” He adds, “We are working now in close cooperation with Latin America, where, for instance, Argentina has doubled its organ donation rate from 6 to 12 donors per million, Uruguay will reach 25 donors per million in 2006, and Colombia has increased organ donation by 50% during the last year.”

Spain attributes its success to its transplantation coordination network. Whereas in the United Kingdom, transplantation coordinators are based in renal transplantation centres, in Spain, they are based at the site of organ donation. The prime function of the Spanish local donation team is to detect potential organ donors within intensive care units. Dr Matesanz says, “The key elements to the Spanish model, which has improved deceased organ donation, is a coordination network at national, regional, and hospital levels.” He explains, “In theory, Spain has a law of presumed consent, but from a practical
point of view, family consent is always asked, and the wishes of the relatives are always respected.” During the past few years in Spain, the family refusal rate has remained stable at around 20%, compared with about 40% in the United Kingdom.

The national and regional authorities fund the first 2 levels, which are the interfaces between the politicians and the professionals, with all the technical decisions about transplantations taken by consensus in a regional council. Dr Matesanz adds, “The third level, that of the hospital coordinator, should be a medical doctor, usually helped by nurses in the big hospitals, who preferably works on a part-time basis and who is located in the hospital.” Continuous brain-death audits are performed by hospital transplantation coordinators.

Dr Matesanz says, “The central office of the ONT acts as the support agency in charge of organ sharing, transport, waiting list management, transplantation registries, statistics, and general and specialised information. It can act to improve the whole process of organ donation and transplantation.”

A significant percentage (about 15%) of organs are retrieved in smaller hospitals without neurosurgery facilities; in these situations, where the whole process cannot be performed, the regional and national offices provide external support. Dr Matesanz explains, “The funding from regional and national health administrations is important, particularly for smaller hospitals. Otherwise, the sustained procurement activity, especially of small, nonuniversity, nontransplantation hospitals, becomes practically impossible.” Another element is the need for constant medical training and education for new and existing transplantation coordinators and for the development of various training programmes for health professionals, specifically dedicated to every step of the process. This includes donor detection and management, legal aspects, family approach, organisational aspects, and management of resources.

Public information is also important in maintaining awareness of the programme among the Spanish population, with hospital and regional coordinators trained in media communication and in managing negative publicity. This training is backed by an adequate legal background on issues such as definition of brain death, organ retrieval after obtaining the consent of the family, and the requirement that there be no compensation for donation or grafted organs.

The successful increase in organ donation during the 1990s has been attributed to the Spanish model approach rather than to any change in Spanish legislation, which has remained unchanged since 1979. One of Spain’s leading cardiac specialists explains that there is close cooperation between ONT and surgeons. Dr Alberto Juffe, MD, PhD (left), head of cardiac surgery at the Hospital Juan Canalejo, La Coruña, explains that there is a single list of recipients for all cardiac transplantation centres in Spain.

He says, “When a heart donor is available, the ONT informs the surgeons or the cardiologists, who are responsible for performing the donor–recipient matching. A single national list of all patients listed assures the fairness of the Spanish mode.” He continues, “Preference for organ allotment is based on the date of inclusion in the waiting list for patients with the same clinical status.”

He adds that if the donor is from an autonomous community with an active transplantation program, the donor remains in the community, with the only exception being for an emergency case in another area. “This arrangement encourages both the medical profession and the community to work together to increase the number of donors, which, in turn, increases the number of transplantations performed in the specific community,” he said.

The Juan Canalejo Hospital’s heart transplantation programme began in 1991 and has performed 529 orthotopic heart transplantations (mean 33 a year). There are 14 heart transplantation programmes across Spain, with periodic meetings between the different groups and the ONT to analyse emerging problems and to discuss the criteria for organ allotment.

Dr Juffe says, “There is absolute confidence on the part of the transplantation teams regarding the ONT. They rely entirely on it to administer the transplantation candidates’ lists. I believe trust is the basis for the sustainability of the system.”

Speaking to Circulation: European Perspectives in Cardiology last year as he stepped down as director of transplant service at Papworth Hospital near Cambridge, United Kingdom, John Wallwork, FRCS, FRCP, acknowledged that UK cardiologists are looking at Spain’s success in obtaining donor organs. He pointed out that organ donation, rather than funding limitations, remains the critical restriction on the number of transplantations. Other European countries are sure to follow.

Mark Nicholls is a freelance medical writer.

References


Viewpoint: Sir George Alberti, FRCP, DPhil

European cardiologists must take the metabolic syndrome seriously.

During the past 2 decades, metabolic syndrome has been controversial throughout Europe, largely because there has been heated debate over whether it exists at all. Sir George Alberti, FRCP, DPhil, emeritus professor of medicine at the University of Newcastle, United Kingdom, helped put together an international definition of the syndrome. He tells Emma Wilkinson, BSc, MA, why he thinks European clinicians should take metabolic syndrome seriously.

The Oxford English Dictionary defines a syndrome as “a group of symptoms or pathological signs which consistently occur together, especially with an (originally) unknown cause.”

It seems churlish by that definition to quibble about whether metabolic syndrome, characterised by visceral obesity, dyslipidaemia, hyperglycaemia, and hypertension, actually exists. But, since 1988, when Garry Reaven, MD, the eminent American endocrinologist, described syndrome X in an article on diabetes mellitus, the very idea of metabolic syndrome has caused much controversy.

Various bodies have attempted to come up with a working definition of the condition, but criticism of their relative accuracy and various discrepancies eventually led the International Diabetes Federation to set up a task force to create an internationally relevant set of rules for identifying people who are at risk of cardiovascular disease and diabetes mellitus. Their definition of metabolic syndrome (see Figure) is central obesity plus any 2 of the following conditions: raised triglycerides, reduced high-density lipoprotein cholesterol, hypertension or treatment for hypertension, raised fasting plasma glucose, or previously diagnosed type 2 diabetes mellitus.

Dr George Alberti is emeritus professor of medicine at the University of Newcastle and senior research fellow at Imperial College, London, United Kingdom; he is also the United Kingdom’s national clinical director for emergency access, and he advises the Department of Health on a number of issues. He was a member of the writing group that was convened to draw up the International Diabetes Federation definition. He admits that there was a lot of squabbling after the final definition was published. However, this has not dampened his fervour for something that he believes has real practical value.

“Whether you have a consensus or not doesn’t matter that much—it helps, it lifts confidence—but what matters more, I suspect, is that there are reasonably common differences that people use to detect people at risk.” He explains, “It’s about saying to patients, ‘you have an increased risk over your fellow man; let’s do something about it.’”

Much of the debate has centred around whether identifying people with metabolic syndrome has any clinical value over currently available risk calculators and tests, such as impaired glucose tolerance. Another issue is whether it’s necessary to label someone with a syndrome so that they will make the appropriate lifestyle changes, when obesity is itself part of the definition.

Dr Alberti believes unequivocally that diagnosing metabolic syndrome does have added value. “This precedes risk calculators and is for people who don’t bother using risk calculators in primary care; in parts of Europe, even worldwide, practitioners often don’t use them. So, this is a way of focusing on people at need and identifying people at risk, without specifically saying how much risk.”

He adds that simply doing a glucose tolerance test would not give a clear picture of someone’s overall risk of cardiovascular disease. “Clearly, it will give you a risk of diabetes, but if you have impaired fasting glucose and also have high blood pressure and an excessive waist measurement, you are much more likely to get diabetes. He continues, “Just measuring glucose or blood pressure is not enough, and the whole point of all this is to make sure that people look at the whole range of risk factors. For the average doctor, this means something that helps remind you of what needs doing.”

In terms of implementing the International Diabetes Federation definition in everyday use, Dr Alberti is particularly outspoken on the benefits of waist measurements in preference to traditional calculations of body mass index. “It’s a damn sight easier to use as a measurement. You don’t have to use a height machine or do sums that are not understood by patients. We are encouraging waist measurement as much as possible.”

The United Kingdom’s National Institute of Clinical Excellence has recently included waist measurement in its obesity guidance, and there has been much talk of including it as standard in the Quality and Outcomes Framework of the United Kingdom’s general practitioner’s contract. However, the International Diabetes Federation’s international definition of the metabolic syndrome did not meet with universal approval.
Dr Alberti points out that continental Europe is way ahead of the United Kingdom in introducing the idea of metabolic syndrome into routine practice. “What we are recommending worldwide is that people keep a close eye on their waist and regularly measure it. We need to educate populations such as South Asians that they need to know they should be checking their own waist measurements.”

“If you read the correspondence pages of European and US medical journals,” says Dr Alberti, “you would be forgiven for thinking that the medical profession is divided over whether metabolic syndrome is a helpful diagnosis; this is not the reality.” In fact, he stresses that the European cardiology profession has been open minded and has almost led the way in acceptance of the existence of the metabolic syndrome. “It’s really been a call to action for cardiologists to take diabetes and those at risk seriously,” he says. “Primary care is slowly coming on board, but by and large, the only people who are really opposed to it are some academics and diabetologists.”

He continues, “There was a group of diabetologists from the American Diabetes Association who didn’t like it because it was labelling people with a disease, which they felt wasn’t helpful. It certainly brought more publicity than we thought would happen. I wrote to the American Diabetic Association to thank them for that,” he says, laughing.

Although Dr Alberti says the official definition is becoming a useful tool in clinical practice, even 2 years after the International Diabetes Federation published it, the issue is by no means closed, and there is still much to learn. “At worst, it’s a convenient way of grouping things together for the benefit of patients, and at best, it is a closely related group of risk factors that have a common aetiological basis that we don’t really understand yet,” he says. “This is very clearly a syndrome—a group of things that cluster together at greater intensity than by chance alone, and no one really disagrees with that.” He concludes, “My hope is that this is a good way of picking up people early in a process, for whom we can then take rapid preventive action—that’s the key. For doctors, it offers a handle to grasp and a course of action to follow.”

Emma Wilkinson, BSc, MA, is a freelance medical journalist.

Reference

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