

String of Pearls and renal failure

Chronic renal failure entails the slow, progressive destruction of kidney tissue and loss of the organ's function. The clinical symptoms depend upon the stage the disease has reached. In line with the global trend, national registration statistics reveal that the number of patients in the Netherlands is increasing gradually. Just over 1900 people in this country began renal replacement therapy (dialysis or transplantation) in 2007. At the end of that year the total number of patients exceeded 13,000, representing just under 0.1 per cent of the population. However, the number of people with early forms of renal failure is many times greater. Estimates from the PREVEND study, a large-scale screening programme, indicate that approximately 5 per cent of the population are in stage 3 or 4 of progression to renal failure.

To a greater or lesser extent, almost all kidney diseases result in loss of renal function. This takes the form of a reduced glomerular filtration rate (a measure of kidney function) and/or albuminuria (loss of protein into the urine). When the kidneys are not working properly, that causes uraemia (a build-up of waste substances in the body) and, eventually, oedema (an inability to dispose of fluids). Early chronic renal failure is often symptomless, which tends to lead to late diagnosis. Even before the patient suffers physical complaints, however, there is a substantially increased risk of developing cardiovascular disease. And that rises sharply as the condition progresses. If the underlying kidney disease is left untreated or the renal failure is discovered too late, there is high risk of the condition entering its end stage.

Chronic renal failure has been divided into five stages, from near-normal (1) to very severely impaired kidney function (5). By this point, the patient requires renal replacement therapy just in order to survive. As our knowledge currently stands, even when the condition is identified and treated early, unfortunately it is not always possible to prevent it progressing to this stage. Medical interventions primarily concentrate upon slowing loss of function and thus postponing the need for replacement therapy. It is also very important to prevent and treat secondary damage to the cardiovascular system and skeleton. In end-stage renal failure, the objective

of the replacement therapy is to keep the patient alive and to retain some quality of life. The two forms of treatment available at this stage are dialysis (haemodialysis or peritoneal dialysis) and transplantation. Dialysis is an intrusive therapy that only improves life expectancy and quality to a limited extent compared with the outlook for patients who have undergone a kidney transplant. But due to a shortage of donors, that option is not available to everyone.

Scientific value

Even before String of Pearls turned its attention to this condition, there were concerted efforts to identify patients suffering from renal failure at an early stage and to improve public information and treatment. These were pursued in consultation with national charities – the Dutch Kidney Foundation, Dutch Diabetes Research Foundation and Netherlands Heart Foundation – and with the Kidney Patients' Association of the Netherlands. There was co-operation with industry, too, in the form of support for clinical studies. With the establishment of the String of Pearls database and biobank, however, doctors and researchers are now able to gain a better understanding of how kidney diseases arise and how renal failure progresses. This should result in better protective measures, and hence improved treatments. Eventually, it may even be possible to develop new therapies tailored to individual patients. Moreover, alliances are to be forged with

other initiatives dedicated to primary and secondary prevention, including major population studies like LifeLines and PREVEND (Prevention of Renal and Vascular Endstage).

Because renal failure can result from a variety of underlying kidney diseases, it has been decided to set up a broad-based biobank. As well as allowing researchers to look at specific conditions, such as polycystic kidney disease and glomerular diseases, this also facilitates investigations not related to one particular ailment. And String of Pearls offers a unique opportunity to link to the existing national registers of dialysis patients (RENINE) and renal transplantees (COTR), which could create a patient monitoring system. There is co-operation at the European level, as well. From its base in the Netherlands, the ERA-EDTA Registry of the European Renal Association/European Dialysis and Transplant Association records clinical data from patients undergoing renal replacement therapy across the continent. In policy terms, this organisation plays an important guiding role for its Dutch partners. For example, it has launched the EU-sponsored NephroQUEST Initiative (Quality European Studies) with the aim of establishing a European network of high-quality registers. Another European initiative, the ReGeNet consortium (Renal Genome Network), maintains a DNA repository containing vascular tissue and phenotype data from more than 25,000 kidney patients. It, too, is co-or-



minated from the Netherlands. There is also collaboration with the EU-funded Genecure project and, at the national level, with the Dutch Society of Nephrology and the Hans Mak Institute for quality of renal care.

About the pearl

Patients with chronic progressive renal failure in stages 2-5 (mild to very severe) are to be registered with String of Pearls. As far as possible, variables are defined in such a way that they correspond with established cohorts and initiatives. Data collected includes age, sex and date of inclusion in the pearl. Also recorded is information gathered during routine clinical examinations, such as height, weight and

blood pressure, as well as the results from laboratory tests of blood and urine. In addition, once a year patients are asked to provide extra blood and urine samples for inclusion in the biobank. These are destined for future DNA and other research.

All data registered with String of Pearls is subject to quality agreements, meaning that it must comply with predefined procedures and guidelines. Thanks to the application of uniform standards for collection, processing and the sharing of data, it is relative easy to link String of Pearls datasets with those from other initiatives using the same standards.

The String of Pearls Initiative

The String of Pearls Initiative is the result of a unique partnership between the eight Dutch university medical centres (teaching hospitals). Founded in 2007 by NFU, the Dutch Federation of University Medical Centres, the initiative gathers clinical data and biomaterials from all the participating institutions so that together, they can promote the ad-

vancement of science, improve patient treatment and encourage the development of new products, as well as strengthening the economic position of biomedical research in the Netherlands. Initially, the project is focusing upon nine groups of medical conditions, its so-called "pearls". In the future, its activities may be expanded to include

others. For more information, you can contact the String of Pearls Initiative at info@string-of-pearls.org.