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Kidney transplant patients need even better aftercare!

Kidney transplantation is the best renal replacement therapy available. Although survival and quality of life are significantly better compared to dialysis patients, transplant recipients nevertheless have a significantly higher cardiovascular morbidity and mortality than healthy people. One recently published study [1] shows current data and derives important conclusions for further long-term improvements in outcomes after kidney transplantation – a highly topical issue, especially for cost reasons and in the event of organ or donor scarcity.

Patients with chronic kidney disease (CKD), and dialysis patients especially, have a significantly higher cardiovascular morbidity and mortality than healthy people. Kidney transplantation is the best renal replacement therapy available. Compared to dialysis patients, transplant recipients have significantly better long-term survival and quality of life [2]. Although their cardiovascular risk decreases, cardiovascular complications are still the main cause of shortened patient and organ survival [3, 4]. One recently published review [5] shows current data and derives important conclusions for further long-term improvements in outcomes after kidney transplantation – a highly topical issue, especially for cost reasons and organ or donor scarcity. The manuscript is a work product of the American Society of Transplantation's Kidney-Pancreas Community of Practice (AST-KPCOP) Cardiovascular Disease Workgroup and appeared in the reputable journal 'Nephrology Dialysis Transplantation'.

Most of the 'traditional' cardiovascular risk factors (such as smoking, high blood pressure, diabetes mellitus, overweight, lipid metabolic disorders/dyslipidaemia) are reinforced by chronic kidney disease. Severe disorders of mineral and bone metabolism may also be included in the multiple consequences and forms of damage resulting from poor clearance of toxins in the body; the imbalance in the calcium and phosphate metabolism leads to bone decalcification and, parallel to that, to an increase in calcium/phosphate deposits in the cardiovascular system. 'The most dangerous cardiovascular diseases (CVD)

include coronary artery and cerebrovascular calcification, cardiac insufficiency, heart valve disease, arrhythmias and pulmonary hypertension', explains Prof. Denis Fouque, Centre Hospitalier Lyon Sud, France, Vice-Chairman of the European Renal Best Practice group of ERA-EDTA and a member of the KDIGO Advisory Board.

After successful kidney transplantation, the detoxification function and also the calcium/phosphate metabolism can return almost completely to normal, but the cardiovascular risk does not decrease to the level of people with healthy kidneys [6, 7]. This is due not only to existing damage, but also to cardiovascular risk factors specific to transplantation. The immunosuppressive drugs that transplant patients need on a daily basis for the rest of their life may cause metabolic disorders such as post-transplantation diabetes (up to 42% of patients), dyslipidaemia (50%), and hypertension (up to 90%) ('de novo traditional CVD risk factors' [8, 9, 10]). Unfortunately, almost one transplant patient out of four continues to smoke [11].

Non-traditional risk factors include metabolic effects of immunosuppressive therapies, chronic inflammatory responses, infectious complications, chronic anaemia, proteinuria, and compromised function of the transplanted kidney resulting in CKD stage 3 or greater [12]).

'Transplantation aftercare is now focused primarily on preventing organ rejection and the side-effects of immunosuppressive therapies', explains Professor Darshana Dadhania, transplantation nephrologist and Associate Professor of Medicine at Weill Cornell Medical Center / New York Presbyterian Hospital, New York – and senior author of the review by AST-KPCOP. 'Early diagnosis and management of cardiovascular disease is a secondary focus at best and due to complex interactions between traditional risk factors, immunosuppressive medications and chronic kidney disease, a traditional approach to cardiovascular disease management is inadequate. '

This may be attributable to a number of causes: whereas a highly specialized nephrological team handles the entire medical management of patients with advanced CKD or on dialysis in the pre-transplantation phase, the transition to the post-transplantation phase is not a continuum, but first of all a 'cut', because perioperative treatment and care is performed by the transplantation surgeons, assisted where relevant by consultants from multiple disciplines. Although patients generally remain in transplantation aftercare after leaving hospital, cardiovascular screening protocols are

variable and do not have a clearly defined, standardized agenda. Aftercare may be provided by surgeons, general practitioners, cardiologists, diabetologists and nephrologists. Professor Janani Rangaswami, nephrologist and Associate Professor of Medicine at Einstein Medical Center/Jefferson University, Philadelphia and the leading author of the review by AST-KPCOP, summarizes by saying that, 'Instead of end-to-end seamless patient care throughout the treatment chain, from CKD to dialysis to transplantation, different medical teams usually assume responsibility for the patient, with a less than optimal approach towards jointly targeting heart disease risk reduction after kidney transplantation.' This fragmentation, of post-transplantation care especially, results in 'snapshots' of care and management processes, and in long-term undertreatment of modifiable cardiovascular risk factors.

There are several things that must change in future. One is that all practitioners, general internists, cardiologists, diabetologists and nephrologists, must recognize that event-free outcome surrounding the time of the transplant surgery is not the only goal and the long-term survival of kidney transplant is dependent on successful management of the patients' cardiovascular disease. 'The multi-disciplinary team of physicians need to work collaboratively to manage cardiovascular disease pre and post-transplant to ensure long-term event-free survival of the patient,' emphasizes Professor Dadhania. In addition, the knowledge gap between the optimal management of cardiovascular disease in a patient with and without CKD must be closed with reliable data and evidence on modification of cardiovascular risk factors; a critical issue that is a consequence of kidney patients generally being under-represented in cardiovascular outcome studies. Ultimately, this is the only way to reach a medical consensus on optimal procedures.

'Instead of the fragmentation hitherto, what we need in order to provide optimized transplantation aftercare is a cardio-nephrological team that acts as a cohesive unit, i.e. a combination of the multi-disciplinary clinical care model and the team approach. In addition to purely nephrological aspects, transplantation aftercare must focus more on cardiovascular risk screening and the respective forms of intervention', emphasizes Professor Rangaswami. 'Only in this way can we continue to improve the survival of patients and the transplanted organs.' Our kidneys filter out toxic waste from the blood and regulate the fluid balance in the body as well as the balance of electrolytes and acid/base amongst others. Kidneys are important organs whose functions most of us take for granted, but when kidneys silently stop working this can create a life threatening situation. Renal replacement therapy, RRT, (dialysis or kidney transplantation) may save

the lives of many patients for years and even decades, as kidney function can be replaced by machines for a long period of time – but patients on dialysis (and transplanted patients to a lesser extent) have shorter life expectancies. This is why kidney failure (end-stage renal disease) should be prevented wherever possible.

A new analysis of data in the ERA-EDTA Registry shows that men are affected by kidney failure much more often than women [13]. In 2016, 26,446 men and 14,820 women started renal replacement therapy. Amongst older patients (>75 years of age), the difference was even more striking: the incidence in men was 2.7 times higher than that in women. 'One can only speculate about the reasons', explains Professor Ziad Massy (Paris), Clinical Nephrology Governance Chair/Chair of the Registry. The protective effects of oestrogens in women and/or the damaging effects of testosterone might cause kidney function to decline faster in men than in women [3]. Moreover, elderly women seem to be more inclined to choose conservative care instead of RRT [3].

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About ERA-EDTA

With more than 11,000 members, the ERA-EDTA ("European Renal Association – European Dialysis and Transplant Association") is one of the biggest nephrology associations worldwide and one of the most important and prestigious European Medical Associations. It supports basic and clinical research in the fields of clinical nephrology, dialysis, renal transplantation and related subjects. It also supports a number of studies as well as research groups and has founded a special "Fellowship Programme" for young investigators as well as grant programmes. In order to involve young nephrologists in all its activities, ERA-EDTA has created the "Young Nephrologists' Platform" (YNP), a very active committee whose board includes members who are 40 years old or younger. In addition, it has established various working groups to promote the collaboration of nephrologists with other medical disciplines (e.g. cardiology, immunology). Furthermore, a "European Renal Best Practice" (ERBP) advisory board was established by the ERA-EDTA to draw up and publish guidelines and position statements. Another important goal of the ERA-EDTA is education: The series of CME courses combined with the annual congress offer an attractive scientific programme to cover the need for continuous medical education for doctors working in the fields of nephrology, dialysis and transplantation. The association's journals, NDT (Nephrology, Dialysis, Transplantation) and CKJ (Clinical Kidney Journal), are currently the leading nephrology journals in Europe; furthermore NDT-Educational is the Society's online educational journal, with free access for all users, as well as being a very important and useful feature of the NDT-Educational "Literature Review". The ERA-EDTA Registry is a large epidemiologic database comparing countries by assessing nephrology practices throughout Europe. ENP, the European Nephrology Portal, is the latest new initiative of ERA-EDTA, where all those interested in the activities of the Society can find everything that is happening, all in one place. Finally, ERA-EDTA is a member of the European Kidney Health Alliance (EKHA), a consortium of patients, nurses and foundations relating to renal issues that actively interacts with the European Parliament. For more information, please visit www.era-edta.org