



Leading European Nephrology

# NEWS

## European Renal Association – European Dialysis and Transplant Association

### High Prevalence of Cardiovascular Pathology in Children on Dialysis

#### Final Report of the 4C study shows alarming results

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The 4C Study enrolled a total of 704 children and adolescents with chronic kidney disease (CKD) in 2010/11 in 54 pediatric nephrology centers in 12 European countries including Turkey. The study investigated the cardiovascular status and CKD progression over 7 years and was funded by the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA).

A comprehensive cardiovascular assessment was performed (including carotid artery sonography, echocardiography, pulse wave velocity and ABPM) and showed a high prevalence of cardiovascular pathology: 26% of children had uncontrolled hypertension, 20% showed LV hypertrophy, 42% elevated carotid intima-media thickness, and 20% increased aortic pulse wave velocity [1].

Moreover, an analysis of advanced cardiac mechanics revealed that a significant proportion of children with CKD showed a subtle impairment of systolic function characterized by lower radial strain, transmural circumferential gradient, and mild cardiac dyssynchrony [2]. These abnormalities were independent of LV mass and ejection fraction and suggest intrinsic structural abnormalities of the heart muscle in children with CKD, putatively related to early myocardial fibrosis.

“These results are alarming”, explains Professor Doctor Franz Schaefer, Heidelberg/Germany, lead investigator of the 4C study. “In adult patients CKD is associated with a high cardiovascular risk, which leads to an impaired survival. The question was, if pediatric patients are at risk, too – and, indeed, they are: We found significant subclinical cardiovascular disease in this cohort.” The study showed that carotid IMT, central pulse wave velocity and LV mass were clearly increasing with time and progressing CKD and were highest in patients on dialysis.

But what could be done to lower the cardiovascular risk of children on renal replacement therapy (RRT)? “We saw that the RRT modality had a significant impact on the change in arterial structure and function. Our findings suggest that pre-emptive transplantation can prevent further deterioration of the subclinical vascular organ damage early after transplantation” [3].



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In addition to these important insights regarding the early development of cardiovascular morbidity, the study identified several markers and potential mechanisms of renal disease progression in children with CKD. In two recent publications the 4C investigators identified independent associations of metabolic acidosis and serum concentrations of suPAR, the soluble urokinase receptor, with more rapid progression of renal failure towards end-stage kidney disease [4,5].

“These are important findings for pediatric nephrology. ERA-EDTA is proud of having funded the 4C study. Thus, we made a significant contribution to investigating the cardiovascular and renal risk of children and adolescents with CKD and, in the long term, to improving their outcome”, commented Professor Doctor Carmine Zoccali, Reggio Calabria, Italy, president of the ERA-EDTA. “The mission of our association is advancement of medical science – and the 4C study is a brilliant example of how ERA-EDTA reaches this ambitious goal.”

[1] Schaefer F, Doyon A, Azukaitis K, et al. Cardiovascular Phenotypes in Children with CKD: The 4C Study. *Clin J Am Soc Nephrol* 2017; 12:19-28

[2] Chinali M, Matteucci MC, Franceschini A, Doyon A, Pongiglione G, Rinelli G, Schaefer F. Advanced Parameters of Cardiac Mechanics in Children with CKD: The 4C Study. *Clin J Am Soc Nephrol* 2015; 10:1357-63.

[3] Schmidt BMW, Sugianto RI, Thurn D, et al. Early effects of renal replacement therapy on cardiovascular comorbidity in children with end-stage kidney disease: Findings from the 4C-T Study. *Transplantation* 2017 (in press).

[4] Harambat J, Kunzmann K, Azukaitis K, et al. Metabolic acidosis is common and associates with disease progression in children with chronic kidney disease. *Kidney Int* 2017 Jul 17. [Epub ahead of print]

[5] Schaefer F, Trachtman H, Wühl E, et al. Elevated suPAR serum levels are associated with progression of kidney disease in children. *JAMA Pediatr* 1017 Sep 5. [Epub ahead of print]

### About ERA-EDTA

With more than 7,500 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 the "Young Nephrologists' Platform" (YNP), a very active committee whose board includes members who are 40 years old or younger. Besides, it has established various working groups to promote the collaboration of nephrologists with other medical disciplines (e.g. cardiology,



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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: several series of CME-courses as well as the annual congress offer an attractive scientific programme to cover the need of 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 online educational journal, open for free to all uses, of the Society as well as the very important and useful feature of NDT-Educational "Literature Review". The ERA-EDTA Registry is a large epidemiologic database comparing countries by assessing nephrology practice throughout Europe. ENP, the European Nephrology Portal, is the latest new initiative of ERA-EDTA: here all those interested in the activities of the Society can find everything that is done, all in one place! Finally, ERA-EDTA is a member of the European Kidney Health Alliance (EKHA), a consortium of patients, nurses, foundations all related to renal issues that actively interacts with the European Parliament. For more information please visit [www.era-edta.org](http://www.era-edta.org)