Invited Editorial / *Davetli Editöryal Yorum*

Global burden of chronic kidney disease and decreased kidney function in Turkish heart failure patients

Global kronik böbrek hastalığı yükü ve Türk kalp yetersizliği hastalarında böbrek fonksiyonlarında azalma

Guliz Kozdag Gold, M.D.

Division of Cardiology, Montefiore Medical Center-Albert Einstein College of Medicine, NY, USA

Chronic kidney disease (CKD) is a non-communicable disease that is a significant contributor to morbidity and mortality. Globally, 1.2 million people were estimated to have died due to CKD in 2017. An additional 1.4 million deaths from cardiovascular disease included impaired kidney function, which represented 7.6% of deaths due to cardiovascular disease in 2017. CKD was the 17th leading cause of death in 1990. Since then, the trend has increased and it became the 12th leading cause of death in 2017.[1] More than 2.5 million people have undergone renal replacement therapy in 2010 and this figure is projected to double to 5.4 million by 2030.[2] However, the impact of CKD worldwide is much greater than renal replacement therapy. Large-scale screening programs carried out in the 2000s in Australia,[3] Norway,[4] and the USA[5] have demonstrated that more than 10% of the adult population had signs of kidney disease. Globally in 2017, there were reported to be 697.5 million cases of CKD. In 2017, the prevalence of CKD was estimated to be 9.1% of the world population, with CKD stages 1 to 2 accounting for 5.0%, stage 3 for 3.9%, stage 4 for 0.16%, and stage 5 for 0.07%.[1]

In this issue of TSCA journal, Dr. Şimşek and coworkers published their subgroup analysis of the Heart Failure Prevalence and Predictors in Turkey (HAPPY) study.[6] The HAPPY study included 4650 randomly selected individuals from the 7 geographical regions of Turkey. The present analysis enrolled 191 subjects from the original cohort with an estimated glomerular filtration rate (eGFR) of less than 60 mL minute/1.73 m^2 with available long-term total and cardiovascular mortality data. The cohort comprised patients with CKD stage 3 through stage 5. The prevalence of CKD stage 3 to 5 was 9.5% in the overall cohort and the result for stage 3 CKD specifically was 9.1%; that is, most patients had stage 3 CKD (184 subjects of 191, 96.3%). The mean age of the patients was 66±13 years.

Abbreviation:

BNP	*B-type natriuretic peptide*
CHF	*Congestive heart failure*
CKD	*Chronic kidney disease*
eGFR	*Estimated glomerular filtration rate*
NT-proBNP	*N-terminal prohormone BNP*

Hill et al.[7] reported that a literature search revealed a CKD stage 1 to 5 prevalence in Europe of 18.38% and a stage 3 to 5 prevalence of 11.86%. The crude stage 3 to 5 CKD prevalence in individuals aged 20 years and older ranged from 1.1% in the Netherlands to 9.9% in northeastern Germany. In adults aged 65 to 74 years, the age and sex standardized prevalence of stage 3 to 5 CKD ranged from 4.1% in Switzerland to 25.4% in northeastern Germany.[8]

Data from the Quality and Outcomes Framework registry indicated that in 2009–2010, more than 1.8 million adults in England had stage 3 to 5 CKD, a diagnosed prevalence rate of 4.3% of the population

Correspondence: Guliz Kozdag Gold, M.D Montefiore Medical Center-Albert Einstein College of Medicine, Division of Cardiology, NY, USA.
Tel: +1-914-361-6194 e-mail: gkozdag@gmail.com

over the age of 18.[9] Hill et al.[7] demonstrated in their pooled data that the prevalence of stage 3 to 5 CKD was 10.06% in China, 11.73% in Japan, 8.14% in Australia and 6.76 % in India-Bangladesh.

According to the statistics of US Center for Disease Control and Prevention, 15% of United States adults, or 37 million people, were estimated to have CKD in the United States in 2019.[10] The prevalence was 5.79% for CKD stage 3 and 0.36% for CKD 4, with an overall prevalence of 14.23% in 2015–2016.[11]

Süleymanlar et al.[12] analyzed 10,000 subjects (CREDIT study) and reported that the overall prevalence of CKD in Turkey was 15.7%, that more women than men were affected, and that increasing age was a significant factor. Stage 3 CKD was most common among individuals aged more than 60 years (1.6% vs. 21.5%). The CKD prevalence was slightly higher among subjects living in rural areas compared with those living in urban areas (16.8% vs. 15.2%; p=0.049). The CKD prevalence was greatest among subjects from the Marmara region (19.7%), followed by the Southeastern Anatolia (18.6%), Black Sea (16.1%), Eastern Anatolia (14.2%), Aegean (13.8%), Central Anatolia (12.6%), and Mediterranean (11.7%) regions. The majority of subjects with CKD were in stages 1 to 3. The prevalence rate for CKD stage 1, 2, 3, 4 and 5 was found to be 5.4%, 5.2%, 4.7%, 0.3%, and 0.2%, respectively.

The 4650 participants in the HAPPY study were 35 years old and older. Therefore, the subgroup study also describes subjects 35 years of age or more. This cohort may not be representative of the prevalence of CKD stage 3 to 5 for all ages in Turkey, but it gives us some idea about the expected prevalence in this age group. The CREDIT study, which also surveyed all 7 regions of Turkey, included individuals who were over 18 years of age. This may explain the difference in the prevalence of CKD stage 3 to 5 between the 2 studies. There may also be other methodological differences related to the selection of subjects in these 2 studies. Age-associated loss of kidney function has been recognized for decades. A progressive decrease in glomerular filtration rate with aging has been reported with wide variability among individuals.[13]

B-type natriuretic peptide (BNP) and N-terminal prohormone BNP (NT-proBNP) levels are usually tested in symptomatic patients suspected of exacerbation of acute congestive heart failure (CHF).[14] DeFilippi et al.[15] observed that the NT-proBNP level was elevated in 56% of asymptomatic patients with CKD. Decreased renal function reduces the fractional plasma clearance of NT-proBNP, and studies have demonstrated associations between graded elevations of these peptides and a deteriorating eGFR or advancing CKD stage.[14] Horii et al.,[16] demonstrated that the NT-proBNP value among patients with cardiovascular disease was associated with the composite endpoint of death and that NT-proBNP appeared to be a useful biomarker for mortality and cardiovascular events. A Chinese study has also reported that among elderly patients with known CAD, the NT-proBNP level was significantly related to the prevalence of CHF and all-cause mortality in patients with and without CKD. There were significant changes in the NT-proBNP level between patients according to the stage of CKD (eGFR: 45–60 mL/minute/1.73 m^2, 526.3 pg/mL; eGFR: 30–45 mL/minute/1.73 m^2, 1531.0 pg/mL; eGFR: <30 mL/minute/1.73 m^2, 4734.7 pg/mL; all p<0.001). The NT-proBNP cutoff associated with mortality was higher in patients with CKD (2584 pg/mL) than in those without CKD (370 pg/mL).[17] In this substudy of the HAPPY research, the majority of the patients had stage 3 CKD (n=184, 96.3%). The mean NT-proBNP level was 423.54±955.88 pg/mL and the mean eGFR was 49.21±8.94 mL/minute/1.73 m^2. Patients who died during the substudy follow-up period had a higher NT-proBNP value than the patients who survived (1060±1629 pg/mL vs. 192±303 pg/mL). The NT-proBNP level in patients with CKD in the HAPPY substudy appears to have a similar trend to the results seen in China.

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