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Review Article

Atrial fibrillation in chronic kidney disease

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ABSTRACT

Atrial fibrillation (AF), one of the most common dysrhythmia in clinical practice, remains frequently in people with chronic kidney disease (CKD). AF is associated with a fivefold risk of stroke, a threefold incidence of heart failure, and an increased risk of death. Co-existence of AF and CKD raises substantially morbidity and mortality. Moreover, the optimal treatment approach (rate versus rhythm control) remains debated due to lack of hard evidence. Oral anticoagulation is challenging, since these patients have both a prothrombotic state and an increased risk of stroke and an inherent platelet and vascular dysfunction and an amplified rate of bleeding. Although promising, the newer anticoagulation agents were not tested in severe CKD. Furthermore, fatal bleeding has been reported.

1. Introduction

Chronic kidney disease (CKD) is associated with an increased cardiovascular (CV) morbidity and mortality [1]. Among CKD patients in the United States, CV mortality is approximately 30 times higher than in matched individuals from the general population and the risk for arrhythmogenic death is one of the highest from any other population [2,3]. Atrial fibrillation (AF) is the most common dysrhythmia in clinical practice and it is independently associated with CV mortality [4]. Numerous studies showed that hemodialysis (HD) patients have a high prevalence of ventricular arrhythmias and an increased incidence of sudden cardiac death [4,5], but for a long time, AF did not cause the same amount of research attention as other area of cardiac pathology [2,6]. In the general population, AF transfers a fivefold risk of stroke, a threefold incidence of heart failure, and an increased risk of death [7].

According to recent European and American guidelines, AF could be classified in two types: valvular or non-valvular [8,9]. Several classification systems were proposed for non-valvular AF, but none accounted for all types of AF [8]. The most widely used classification divides AF into paroxysmal and non-paroxysmal, including persistent or permanent types, based on the duration and chronicity of each episode [10].

2. Epidemiology of AF in non-dialysis CKD, dialysis, and transplantation

In the general population, the prevalence of AF is estimated to range between 0.4 and 1% depending on age; its prevalence doubles with each decade of age, reaching approximately 8% in patients over 80 years old [11]. CKD, defined as either pathological albuminuria (>30 mg/24 h) or decreased GFR (<60 ml/min/1.73 m^2), is associated with a higher incidence and prevalence of AF, compared to the general population [12,13].

Data on the epidemiology of AF in patients with CKD are limited. The incidence of AF was increased in hypertensive patients with CKD (adjusted HR 2.18, 95% CI 1.2–3.9), but the relationship was statistically significant only among patients with advanced CKD (stages 4 and 5) [14]. Additionally, a significant and progressively higher risk of incident AF starting with mildly decreased kidney function to more advanced renal failure was reported in the Atherosclerosis Risk In Communities cohort (HR 3.2; 95% CI 2.0–5.0 in CKD stage 4 and 1.6 95% CI 1.27–2.13 in CKD stage 3) [12]. Similarly, data from a Medicare cohort estimated the 2-year incidence of AF at 12.2% for patients with CKD stages 1 and 2 (that is, patients with pathological albuminuria and GFR ≥60 ml/min/1.73 m^2), at 14.4% for stages 3–5, and 13.4% for unknown stage, compared with 7.5% for patients without CKD [15]. In a recent large cohort of African-American and white US adults, CKD was associated with an increased prevalence of AF; the prevalence of AF was highest among those with stage 4 or 5 CKD, but the association persisted across all of the CKD stages [16].

In end-stage renal disease (ESRD), the prevalence of AF varies considerably among studies, between 13 and 27% [17–19]. The USRDS registry reported a prevalence of 13% in patients on HD and 7% in patients undergoing peritoneal dialysis [2,5,20]. Importantly, in the last 15 years, the prevalence of AF increased more than 3-fold, from 3.5% to 10.7% in HD most probably associated with higher life expectancy [6]. Recent data retrieved from Taiwan's National Health Insurance Research Database showed an incidence rate for AF of ~12.1/1000 person-years in patients with ESRD, which was 1.66-fold higher than in CKD patients and 2.42-fold higher than in control patients [10].

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AF was reported in approximately 6% of patients undergoing renal transplantation and was associated with significantly higher post-transplant mortality, graft loss, and stroke [21]. Following renal transplantation, AF is common, affecting almost 7% of renal transplant recipients in the first 3 years post-transplantation [22]. The incidence of AF is higher in the immediate peri-transplant period, associated probably with surgical stress, anesthesia, and excess catecholamine production [23]. Age, previous myocardial infarction, and simultaneous liver/kidney transplant independently predicted peri-operative AF [24]. After approximately 17 months, AF declines below the adjusted prevalence recorded in patients on the transplant waiting list. A possible explanation is regression of left ventricular hypertrophy, a known determinant of arrhythmias in dialysis patients, over the first 2 years post-transplantation [22]

3. Classical and novel risk factors for AF in CKD

The classical risk factors for developing AF include age, hypertension, valvular disease, (ischemic) cardiomyopathy, diabetes mellitus, or thyroid disease. However, in recent years, other factors playing a role in the genesis of AF have gained attention, including sleep apnea, inflammation, obesity, or genetic factors [25].

The prevalence of AF increases with *age* and is highest among patients older than 80 years, both in the general population and in CKD [26,27]. In 2006, the USRDS registry reported a prevalence of 13.2% in HD patients aged 65–74 years, 19.2% in those aged 75–85 years, and 22.5% among those >85 years of age [2,6]. In this regard, the prevalence of CKD also increases with aging: 37% in patients aged 65–74 years, 48% in those aged 75–79 years, and 60% among those >80 years of age [28]. Thus, elderly people with both CKD and AF are becoming increasingly frequent—see Fig. 1.

Caucasians have a drastically lower risk of AF Native Americans (−47%), Afro-Americans (−39%), or Asians (−18%) [6]. Genetic polymorphisms that encode atrial membrane stability or conduction pathways resulting in a different susceptibility to development of AF could explain these important racial differences [29]. Further studies are needed to determine whether genetic factors underlie geographical differences in AF incidence. In a comparative analysis of the incidence of AF in different countries using data from DOPPS, a wide range of variation was noted, fluctuating from 0.5/100 person-years in Japan and 0.73/100 person-years in Taiwan to 3.0/100 person-years in Sweden [10,30].

AF and CKD share several common risk factors (e.g., hypertension, diabetes, preexisting cardiovascular disease, obesity, metabolic syndrome). AF is highly correlated with atherosclerotic disease (particularly coronary artery disease), degenerative valvular disease, and subsequent chronic heart failure. Conversely, AF can manifest or aggravate existing heart failure [4]. Most of these factors are related to electrical and structural remodeling of the right and left atria, which could have a significant role in the promotion and perpetuation of AF [31]. The case of hypertension merits specific comments as may represent a case of reverse epidemiology. Whereas hypertension is associated with AF in the general population, this association is weaker in ESRD

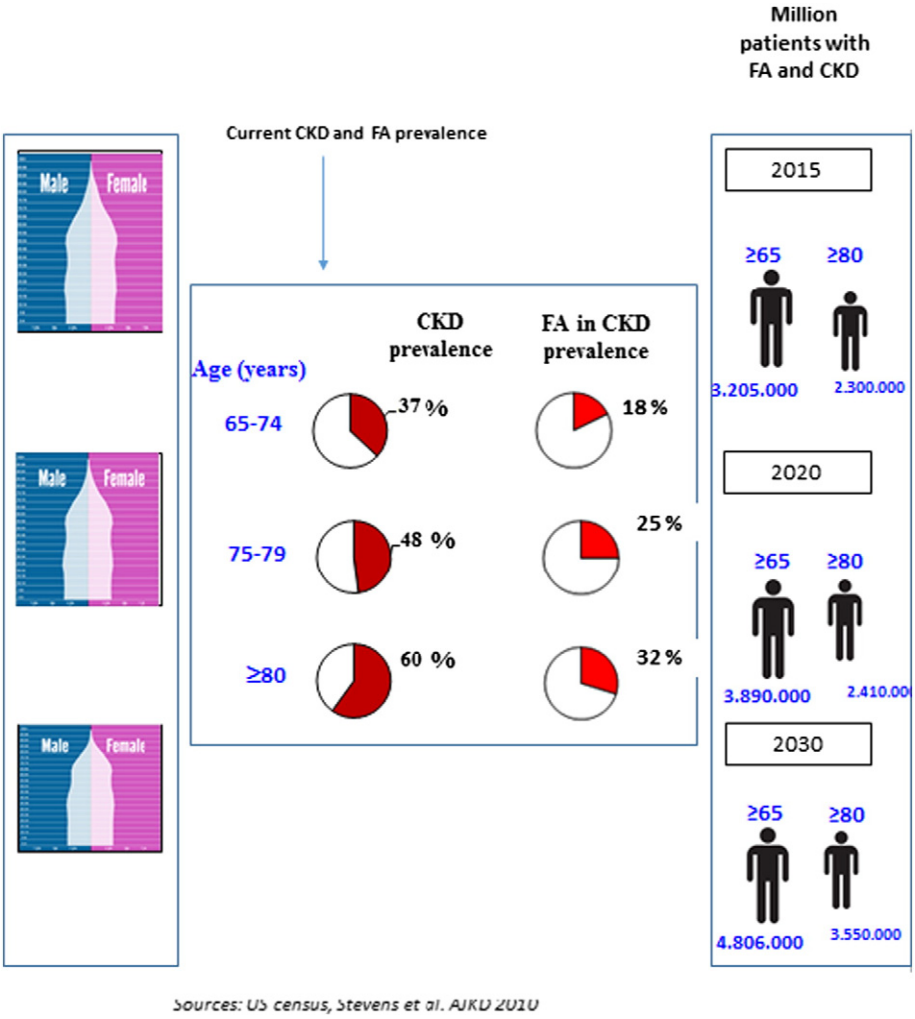

Fig. 1. Increasing prevalence of the CKD-AF combination as a consequence of population aging. The model assumes that the age-adjusted prevalence of AF and CKD will remain stable over the next 15 years. Sources: US census, Stevens et al. AJKD 2010.