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EDITORIAL

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Tackling chronic kidney diseases in the third millennium in Italy. How can digital health help the National Health System?

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Introduction

Chronic kidney disease (CKD) is a widespread and expanding disease. In the USA, it is estimated that more than 13% of the adult population (over 20 million individuals) has CKD in its various stages of severity, and the prevalence of CKD is expected to reach 17% in the next 10 years (1). In Italy, the *prevalence of CKD is around 7.5% of the adult male population* (aged between 35 and 79 years) and 6.5% of the adult female population (aged between 35 and 79 years) that accounts today for about 2.5 million people affected by a degree of CKD (2). The high risk of death (mostly due to cardiovascular causes) associated with CKD, the epidemic dimensions (comparable to those of type 2 diabetes mellitus), and the high social and economic costs associated with renal replacement treatments (RRTs) make CKD one of the main topics in prevention plans and health planning.

The causes for the increase in the prevalence of CKD include aging of the general population, type 2 diabetes mellitus, metabolic syndrome, arterial hypertension, congestive cardiovascular compensation, cardiorenal syndrome, and increased survival of the population suffering from multiple comorbidities (3).

The increasing cost of CKD

Although only a small portion of people with CKD needs RRT (about 0.8% of the population – 50,000 people in Italy), the high costs of these treatments raise serious questions about future sustainability (4). Even though it is difficult to estimate the overall expense of dialysis treatments, the data that emerge from the literature show that in Italy a single hemodialysis session has a direct cost of around €280, while the peritoneal dialysis service has a direct cost of about €83. This means that approximately €43,800 per patient on hemodialysis and €29,800 per patient on peritoneal dialysis are spent each year. Considering the indirect and transport costs, the estimate of the real annual cost for each RRT could be much higher (5).

Transient changes in kidney function (acute kidney failure – acute kidney injury [AKI]) complicate between 2.9% and 23.2% of all hospitalizations (6). This great variability depends on several factors such as the definition of AKI, the data source used, and the case mix considered in the various published studies. Regardless of the methodological considerations underlying the great variability of the prevalence estimates of the phenomenon, the most striking data are that the episodes of AKI, including those that need RRT, are constantly increasing in developed countries. In the index period of 1988–2002 (7), an increase in the incidence of AKI was observed in North America. Indeed, AKI incidence increased from 610 cases (40 of whom needed RRT) to 2,880 cases (270 of whom needed RRT) per million people (pmp) (approx. fourfold increase). The same growing trend has been maintained also in more recent observations and in Europe. In Italy, although there is no system for detecting the phenomenon on a national basis, it is estimated that in the 5-year period between 2007 and 2012 the incidence rate of AKI in need of dialysis treatment doubled, moving from 209 to 410 cases pmp, of which about a third were intensive care unit (ICU) patients (8). Parallel to the increase in cases, recently there has been a change in the scenario with a relative increase in patients with AKI in need of RRT (AKI-D) hospitalized in nonspecialist wards. In the same index period between 2007 and 2012, the ratio of patients with AKI-D hospitalized in nephrology compared to patients hospitalized in nonspecialist wards went from 1:1 in 2007 to 1:2.4 in 2012 (8). In addition to the increase in resource consumption, this phenomenon challenges the current organizational model of hospitals both to ensure better patient care and to improve the efficiency of the system. Indeed, the onset of AKI complicates the hospital course by increasing the time of the hospitalization and worsening both the intrahospital and medium- to long-term prognosis (increased risk of occurrence

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of CKD among those who develop AKI) and increases the consumption of resources.

The role of an interdisciplinary team

For the management of the patient with acute or chronic reduction of renal function, identification and early treatment of the renal function deficiency are required. In these regards, dissemination of diagnostic and best care practices with the provision of interdisciplinary collaborations between nephrologists, general practitioners, and other specialists such as cardiologists, diabetologists, nutritionists, psychologists, and nursing staff expert in kidney diseases is desirable. However, some lines of evidence suggest better results in terms of clinical outcomes and resource allocation when nephrologists lead the multidisciplinary team required to provide the nephropathic patient with the best care. In two English studies (9, 10), it was observed that hospitals that did not have the nephrology service had a higher 30-day mortality than hospitals equipped with this service. In particular, in hospitals not equipped with specialized personnel, there was a 55% higher mortality (9, 10). In another Swiss study, the importance of timing of nephrological consultation was documented. Patients who had had "early" nephrological consultation showed a lower need for emergency dialysis treatments (24% vs. 31% of those with late intervention) and a lesser need to continue dialysis treatment after discharge (2.6% against 7.2%) than peers receiving a "late" consultation (11). Not only was early specialist intervention associated with better renal functional recovery but also the length of stay and hospital mortality appeared better in patients with "early" intervention of the nephrologist. Despite this evidence, an alarming fact reported in these works is that, even in the centers with nephrology service available, a large part of the AKI episodes go unrecognized and only about a quarter of patients are seen or referred to the nephrologist, reiterating the need for monitoring systems able to perfect the timely interaction of different specialists (9-11).

The importance of telemedicine and artificial intelligence

The challenge facing the National Health Care System (NHS) is clear: limited resources and increasing health demand. What are the solutions? Dehospitalization of the chronically ill and implementation of technology represent two potential approaches to the problem. However, while the medical literature confirms that the RRT management in centers on the territory and at the patient home (where possible) is equally effective but cheaper, implementation of these strategies is often hindered by the absence of a caregiver able to assist the patient during dialysis. Telemedicine and artificial intelligence (AI) algorithms can be valid solutions to guarantee an effective remote control of the treatment. Despite the great progress made and the numerous applications of biofeedback systems in the world of dialysis, how and when to integrate all these data sources still appear laborious and suboptimal. In this sense, the application of AI algorithms could help and improve the correct and early identification of patients at risk or alternatively with initial deterioration of renal function as well as improve remote dialysis management (3).

Some applications of AI to the kidney disease world have already been attempted. Tomasev et al (12) developed a machine learning model (deep recurrent neural network model) for the prediction of AKI in patients hospitalized for various reasons. The first results document that the model was able to predict 55.5% of AKI risk and 90.2% of AKI-D episodes. Although the model performed well, its large-scale interpretation and application still appear problematic as the three factors that explained most of AKI risk were: (i) prehospitalization creatinine; (ii) the value of serum creatinine during hospitalization; (iii) the calcemia value during hospitalization. In addition, the model had a 48-hour lead time and a 2:1 ratio of false alarms. Adhikari et al (13) developed a model for postoperative AKI prediction. In this model, data derived from a validated risk score (MySurgeryRisk AKI model) were integrated with clinical and physiological data recorded during surgery. This model also gave encouraging results (40% of the patients identified as high risk by the MySurgeryRisk AKI model were correctly reclassified at low risk), confirming that the integration of different data sources (laboratory, clinical, and physiological) represents the frontier of the next future for the creation of AI models able to improve both the patient outcome and the clinician work.

Kuo et al (14) developed a convolutional deep learning (AI) model for the prediction of glomerular filtrate and the stage of renal failure from ultrasound images of the kidneys. Even this effort, while providing encouraging results, needs further development in order to be implemented in the clinic.

Another machine learning application has been attempted to facilitate the reading of kidney biopsies (15). After machine training, the algorithm was able to identify 92.7% of the glomeruli present in the histological preparation, with a false positive frequency of 10.4% and an intraclass correlation of 0.94 when compared to expert pathologists.

Putra et al (16) proposed an Artificial Neural Network (ANN) model for the prediction of clinical events during the hemodialysis session with encouraging results (average accuracy 93.5%), suggesting the potential of new technologies in the world of dialysis.

The road is still long and winding

Although AI appears to be a potentially useful tool (3) to overcome the challenge facing nephrologists, the development of this approach in nephrology is still limited by the great heterogeneity (and not always easy availability) of clinical data to be integrated to optimize performance of these models. The need to "train" these systems on a wide range of cases, representative of the entire population, represents a current limit for the large-scale implementation of the AI algorithms developed to date and for the personalization of individual patient treatment.

In conclusion, the aging of the population and the chronicity of numerous pathologies seem to justify the epidemic of CKD and the increase in episodes of acute renal failure. The challenge that the NHS is preparing to face in the medium and long term appears implausible in light of the limited resources available. New technologies, including AI, represent an interesting and potentially useful tool to optimize efforts in the field and improve the management and treatment of nephropathic patients. It is therefore desirable to multiply efforts to optimize and validate new technologies in nephrology.

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