Background

IgA nephropathy (IgAN) is a primary glomerulonephritis (PGN), characterized by the deposition of IgA1 in the glomerular basement membrane, and is one of the most important causes of chronic renal failure in adults (1, 2). After 10 to 20 years of follow-up, the rate of progression to ESRD is 10% in China (3). Globally, about one-third of PGN patients have been diagnosed with IgAN, and the proportion is higher in the south of Asia and the Mediterranean region. It is estimated that the number of adult patients with IgA nephropathy is about 4.6 million in China (4). IgA nephropathy is more frequent in young adults. The patients aged 25-44 years account for 51.1%~67.0% of all patients, resulting in huge loss of productivity to the society (5).

For patients progressed to ESRD, the average medical expenses per patient (22) (PD, hemodialysis) and renal transplant (RT) bring heavy economic burden to families, the society, and the government (6).

Due to the large number of IgAN patients and the heavier economic burden of treatment after disease progression, it is essential to predict the lifelong economic burden of IgAN patients in China.

Methods

Model Construction

A three-stage (IgAN, End-stage renal disease/ESRD, Death) Markov model was developed to estimate the total economic burden of IgAN patients with a lifespan (40 years) time horizon from society perspective in China.

The patients enter the IgAN state, and then they can either remain with IgAN progression to the ESRD or die in each cycle of the model. Patients who have progressed to ESRD cannot return to IgAN and can only remain in the ESRD state until the end of life. The death was the absorption state (Fig. 1).

The simulation for each cycle was 1 year duration with half cycle correction, and the discount rate was 5%.

The model was constructed and analyzed using Microsoft Excel 2016.

Baseline characteristics

The baseline characteristics of IgAN patients used in Markov Model were based on a retrospective cohort study of IgAN patients in China and IgAN nephropathy, as shown in Table 1.

The age of kidney biopsy was 33 years, which was simulated to reach the national average life expectancy of 78 years after 45 years simulation (life-long) (7).

Transition Probabilities

The transition probabilities of IgAN state to ESRD state were based on Lee's study (8), presenting in Fig. 2. The best fit distribution for renal survival curve simulation was selected according to Akaike information criterion (AIC) and Bayesian information criterion (BIC).

The age-adjusted once cumulative rate of IgAN was assumed equally to that of the natural population).

The all-cause mortality rate of ESRD was calculated by adding ESRD-associated mortality to natural mortality. ESRD-associated mortality was obtained from the published literature (9).

Patients with IgAN could achieve remission or not after initial treatment. Based on the literature (10), the 1-year remission rate was 74.04% and 18.36% respectively.

Patients after remission could relapse, and the 6-month relapse rate was 15.5% based on the published literature (11).

Interventions

Based on literature review and experts’ survey, 31.3% of patients use Renin-Angiotensin- Aldosterone System (RAAS) inhibitors + traditional Chinese medicine (TCM); 42.6% use RAAS inhibitors + TCM + glucocorticoid (GC) and 14% use RAAS inhibitors + TCM + GC + immunosuppressant (IS).

Patients with IgAN received treatment and remission according to the literature (12), the treatment costs of patients with IgAN and ESRD per capita (13) are projected for long-term analysis.

Adverse Events

Few studies have reported adverse events (AEs) of RAAS inhibitors, so this study mainly considered the AEs of Grade 3/4 severity of glucocorticoid and immunosuppressants, such as diabetes, infection, head neural head and insomnia (14, 15).

The costs of AEs treatments in patients with IgAN were mainly derived from literature and expert survey (16).

Results

Base-Case Result

The total annual survival rate of IgAN patients at the 10-, 20-, and 40-year ages were 63% and 64% based on the results from cohort, and projected to 30% -40% and 45% years were 51.3%, 41.3%, and 31.3%, respectively (Fig 2). The simulated lifetime medical cost per patient was ¥4,158,360 (Fig. 3). The average lifetime medical cost per patient with IgAN in RMB 1,456,876 (2015, 2019 US dollars) (exchange rate 1.85) (Fig. 4) was from society perspective in China.

More than 80% of total cost was attributed to the treatment cost of ESRD.

Sensitivities Analyses

Cost, transition probability, and other clinical parameters were considered in univariate sensitivity analyses. The parameters ranged from 20% of the base case, and direct medical costs range from 0% to 8%.

Univariate sensitivity analysis showed that the three main factors were the discount rate, direct medical cost of ESRD and average annual all-cause mortality of ESRD (Fig. 6). For example, the increment of the discount rate was 5%, the direct medical cost of ESRD was ¥0.5 million, and the average annual all-cause mortality was increased by 20%.

Scenario Analyses

If the transition to ESRD could reduced by 10%, 20%, 30% by a new intervention compared to current IgAN treatment, 4, 6, and 14 years of ESRD will be delayed (Table 2).

Conclusion

From society perspective, the lifelong cost of IgAN per patient is about 1.42 million in China, bringing heavy economic burden to the families, tenants and healthcare system; In the scenario analysis, if a new treatment could reduce the risk of IgAN disease progressed to ESRD by 10%-30%, the time of progression to ESRD was significantly delayed by about 4-14 years;

It has a huge unmet medical need to reduce the risk of patients progressing to ESRD, and then further reduce the financial burden on the healthcare system and improve patients’ quality of life.

References