Hemodialysis Access Management in China

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The Current Condition of CKD in China

Rapid economic development, lifestyle changes and more aging population in China have led to higher incidence and morbidity of chronic disease in the past 30 years. Chronic kidney disease (CKD) is one of these examples. The statistics show that the incidence in China has reached 10.8 % with notable differences among regions. The incidence in the north (16.9 %) and the southwest (18.3 %) is higher than that of any other regions in China. It is estimated that there are about 119.5 million patients with CKD, but only 12.5 % of them aware of that, of which approximately 2 % (2–3 million) of CKD patients suffer from end-stage renal disease (ESRD) which requires hemodialysis [1].

In the past 10 years, the increasing incidence of hypertension, obesity, type 2 diabetes mellitus and environmental factors have exacerbated the burden of CKD in China [2–3]. Data from the Chinese Renal Data System, a national registry system for patients undergoing dialysis reveals that glomerular disease (57.4 %) is the most common cause of ESRD, followed by diabetic nephropathy (16.4 %), hypertension (10.5 %), and cystic kidney disease (3.5 %). However, a shift in the epidemiology of kidney disease has been reported in China. The leading causes of CKD among elderly Chinese patients are diabetes mellitus and hypertension, rather than glomerular disease. Moreover, it is possible that the prevalence of diabetic nephropathy in China will continue to rise, given the rapid increase in the prevalence of diabetes mellitus in this country [4]. The registry number in Beijing and Shanghai of ESRD on maintenance hemodialysis (MHD) was 107.3 and 114.8 per million people (PMP) in 2011. The mean age of patients with MHD becomes older. Cardiovascular and cerebrovascular events are the leading cause of death in those patients, and death due to infection decreased.

The Burden of HD in China

Hemodialysis, as a primary and effective treatment for ESRD patients, is a great challenge for individual and public health system due to the huge financial burden [5]. A survey by the Chinese Society of Blood Purification estimated that the prevalence of patients with ESRD on maintenance hemodialysis or peritoneal dialysis was 71.9 per million population (PMP) in mainland China in 2008, with an annual growth rate of 52.9 %. In Taiwan, the prevalence of patients with ESRD on dialysis reached 2584 PMP in 2010, whereas rates of 1106 PMP and 1870 PMP

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were reported in Hong Kong and the USA, respectively. The lower rate was largely due to unaffordable health care, especially in rural regions. These issues are currently being resolved according to the new Chinese health reform strategy. The government aims to expand health insurance to cover more chronic and critical diseases, focusing on reducing the financial burden for the individual patient. ESRD was among the list of major diseases control in 2012, which could promote and improve the life quality of hemodialysis patients in China.The medical insurance system in China includes three parts: 1. The basic medical insurance for urban workers both in cities and towns; 2. The basic medical insurance for urban residents, which covers all children, students and elderly people without employment; 3. The New Cooperative Medical Scheme (NCMS), which covers all residents of rural regions. By 2011, more than 1.3 billion people had joined the three basic medical insurance systems, and the total coverage rate increased from 87 % in 2008 up to 95 % in 2011. Both hemodialysis and peritoneal dialysis are covered by the three basic medical insurance systems, but the rate of reimbursement varies from 50 to 90 % according to different regions and socio-economic development [6].

Hemodialysis Centers and Access Usage in China

The distribution of hemodialysis centers in China are not balanced. Centers are more popular in developed areas, such as east and south regions and metropolises like Beijing, Shanghai, Guangzhou etc. However, the situation of unbalanced distribution of hemodialysis centers and improper access selection have improved a lot due to the publication of hemodialysis management guideline of Chinese medical instructions, which was issued by the Ministry of Health of the PRC in 2010.

At present, no specialist is specialized for the establishment of hemodialysis access in China. Many doctors including nephrologist, vascular surgeons, urologists, orthopedic surgeons, microsurgery doctors and cardiac surgeons can perform the operation. The lack of specially trained physician team for creating access is one of the main reasons for varied outcomes between various regions.

The first hemodialysis access selection for hemodialysis patients varies widely in different hemodialysis centers [7–10]: In Shanxi Province, the ratio of autogenous arteriovenous fistula (AVF) for the first dialysis access is 41.2 % and non-tunneled catheter (NTC) or non-cuffed catheter (NCC) is 53.3 %. In Shanghai Changzheng Hospital, the ratio of NTC/NCC for the initial dialysis access among the 667 patients is 81.2 %, tunneled cuffed (TCC) is 4.20 % and AVF is 14.54. As for the 435 MHD patients, the ratio of AVF is 83.91 %, TCC is 13.56 %, NTC/NCC is 1.84 %, and the arteriovenous fistula graft (AVG) is only 0.69 %. In Beijing, the ratio of AVF in initial dialysis patients ranges from 21 to 30.2 %. The single-center data in Shenzhen shows that the ratio of AVF is 95.23 %, TCC is 3.40 %, NTC/NCC is 0.68 %, AVG is 0.68 %. Another single-center data in Zhejiang Province shows that only 73 patients (8.73 %) use AVF as the vascular access for the first dialysis, the rest of 763 patients (91.27 %) use central venous catheter. Six months later after dialysis, 542 patients (81.5 %) use AVF as permanent vascular access, 123 patients (18.5 %) use TCC and 55 patients have converted to peritoneal dialysis.

The lower application rate of AVF on initial HD patients is affected by many factors, such as no formal follow-up for CKD patients by nephrologist more than one year and whether the patient has been advised to create AVF in advance [11]. Literature shows a high AVF application on nephrology patients who are followed up over 4 months than those who are followed up less than 1 month. The rate of AVF application in patients whose follow-up period is more than 12 months, is higher than that of the period between 3 and 12 months. The longer follow-up period the higher AVF utilization, and multivariate analysis also shows the earlier follow-up the higher AVF application. In addition, the education of dialysis access to the nephrology patients (especially CKD 4 patients)

is very important for AVF utilization in the initial dialysis. The awareness of CKD patients and the rate of receiving formal medical treatment are lower in China. Most patients have already reached the stage of uremia when they come to the hospital for the first time. Meanwhile, the etiology for the ESKD patients is DM and hypertension, therefore, the patients generally will ask for help from the outpatient department of endocrinology, cardiology and traditional Chinese medicine instead of from nephrologist. As a result, the current situation remains that the patients hardly receive any follow-up or advice of creating an AVF in advance by nephrologists.

The hemodialysis access, such as AVF, AVG and central venous catheter (NTC and TCC) are all available in China. According to K-DOQI, CPM, FFI guidelines, the first choice and recommendation is AVF, followed by AVG, and the final choice is central venous catheter. The lower ratio of AVF maturation and application is affected by many factors, such as the poor follow-up on ESRD patients, unbalanced technique in access creation between regions and doctors, as well as high incidence of diabetes and peripheral vascular disease (PAD). A consensus reached by Chinese experts about hemodialysis access was published in 2014 [12], aiming to improve the patients' awareness and standardize the application. The target proportion of AVF usage is over 60 % in the initial dialysis patients, over 80 % in MHD patients.

Chinese Experts Consensus on Hemodialysis Access in China: Timing of Surgery

Recommendation 1. Patients should receive a variety of healthy information about renal replacement therapy, including kidney transplantation, when GFR < 30 mL/min/1.73 m^2 (CKD4, MDRD formula). 2. GFR < 15 mL/min/1.73 m^2, serum creatinine >6 mg/dl (528 μmol/L) (GFR < 25 mL/min/1.73 m^2, serum creatinine >4 mg/dl (352 μmol/L) in diabetics), patients should take hemodialysis as renal replacement therapy, and are expected to accept dialysis in the next 6 months, AVF should be performed. However, AVG can be postponed to 3–6 weeks before dialysis. 3. Patients who have severe symptoms and have difficulty to control with support treatment should create AVF as soon as possible; residual renal function is not a necessary indicator.

Evaluation

Detailed preoperative examination is of great importance for fistula maturation. Previous central venous catheters or pacemaker placement is associated with significant incidence of central venous stenosis. A history of arterial punctures may have caused vascular injury. Advanced age and diabetes patients with peripheral artery disease are at increased risk of hand ischemia after access creation. Preoperative ultrasound will be helpful for patients with poor vessels condition. However, if the Doppler exam is not conclusive, venogram is indicated for those cases.

Surgical Approach

Local anesthesia injection (1 % lidocaine) is the preferred modality for AVF, and axillary block for AVG. According the guideline, AVF is first-line recommended, followed by AVG. The most practical anastomosis site for AVF is cephalic vein–radial artery end-side anastomosis, followed by basilic arteriovenous fistula, and cubital–brachial artery fistula. The principle of location is upper extremity priority to lower, distal priority to proximal, non-dominant priority to dominant arm.Fistula established on arm: wrist AVF is the first choice, then AVF on forearm (cephalic-radial, transposition of basilic vein to radial artery, transposition of basilic vein to brachial artery, transposition of cephalic vein to brachial artery), the final is AVF on elbow (brachial–cephalic, brachial–basilic, brachial–antecubital). Any type of AVG can be performed after bilateral forearm venous depletion. The forearm commends firstly because of the enlargement venous on upper arm is helpful for the upper arm AVG.

Standards of Fistula Maturation and Judgment

The definition of AVF maturation is easy to puncture with minimal bleeding risk and can provide sufficient blood flow during the entire process, and can also withstand more than three times a week puncture for dialysis. Inadequate blood flow is defined as: the pump control blood flow is less than 200 ml/min in dialysis. The judgment of maturation: Physical examination: thrill well at anastomotic site, no enhancement, weakening or disappearance; the shape of fistula vein goes straight lines, superficial, easy to puncture, sufficient area for puncture, and good elasticity of fistula vascular wall. Natural blood flow over 500 ml/min, the inner diameter greater than 5 mm, the depth from skin less than 6 mm.

Timing and Method of Access Puncture

It is recommended to puncture 8–12 weeks after surgery, at least 1 month after the fistula mature. Note the aseptic principle when doing dialysis. The order of puncture is from the distal to proximal, with stepped or button-type puncture method and avoid the anastomosis area. Needle selection: in the initial stage, it is recommended to use a small (17 G) needle and a lower blood flow (180–200 ml/min). After the dialysis, immediately perform compression when the needle comes completely out, with pressure adjusted to maintain a balance between the thrill and bleeding. Usually puncture the access graft at 2–3 weeks after surgery and the local swelling is subsided; before puncture, the configuration, thrill and palpation should be confirmed. If possible, recommend 3–6 weeks after the procedure to do a puncture. Direction of flow in synthetic grafts should be determined, the needle direction of "pull" and "return" are all to the apex. The main problem within the fistula is the lower proportion of maturation. One of the reasons is the high ratio of central venous catheterization (CVC) in ESRD patients due to subjective or objective factors. The early complications of fistula are often related to surgical/technical factors, including thrombosis, bleeding, infection, hand ischemia and paresthesia from nerve injury during the procedure. Late complications are related to dialysis practice and needle puncture. The most common are vascular stenosis, thrombosis, infection, false/true aneurysm, and swollen hand syndrome, and seldomly high-output heart failure [13]. Postoperative Doppler examination is very important for detection of complications. Stenosis often occurs in or near an anastomosis, previous intravenous catheter sites, and repeated puncture points. PTA as an innovative treatment can relieve the stenosis and prolong the life of fistula. Recently reported from the literature, balloon angioplasty also can promote fistula maturation. Thrombosis can occur at any level of the vein. It often starts at a stenosis or aneurysm site, if it locates at the anastomosis and the proximal vein is still open, re-creation of the fistula a few centimeters up from the anastomosis site is the usual practice. Also it can be declotted and the stenosis corrected with a patch or interposition graft. Anti-platelet drugs are helpful for the prevention of thrombosis, research shows more than 1 year duration aspirin can reduce the risk of fistula dysfunction, another shows that clopidogrel may reduce 37 % fistula thrombosis [14]. The incidence of ischemia in AVF is 19.7 %, mainly is grade I ischemia (71.4 %), mostly can be recovered after conservative treatment. However, the reason is not clear, maybe it relates to the advanced age, women, smoking, diabetes, hypertension, and high location fistula.

Arteriovenous Graft (AVG)

The proportion of AVG access ranges from 0.68 to 5 % in various dialysis centers in China. Most dialysis physicians take NCC/TCC as the second choice for patients who do not have suitable vein for AVF. Although many types of grafts are available, including autologous, allogeneic, xenograft and artificial vessels, ePTFE is still the preferred graft in practice. Most procedures of AVG are performed in big hospital by vascular surgeons. The guidelines of NKF-KDOQI suggest graft access shall be created at 3–6 weeks before dialysis,

as the maturity period is not more than 4 weeks. The condition in China is that most patients have accepted CVC in initial dialysis, thus leading injury to the central vein and also high percentage of central venous stenosis. If a subclavian stenosis is demonstrated or suspected, venogram should be performed to determine the extent of the process. The AVG creation in hybrid operating room is necessary for those patients, the inflow and outflow can be detected and deal with by endovascular techniques, thus improving the long-term patency rate of grafts.

The common complications of AVG are thrombosis and stenosis. They are also the main causes for graft dysfunction. Thrombosis can be classified into two types, early and late thrombosis, according to the time of post procedure. Less than 14 days is defined as early thrombosis, which is related to the patients' characteristics (hypotension, diarrhea, dehydration, diabetes, advanced age) and dialysis early. Thrombolysis can be used when rule out the curved graft, sometimes should combine with PTA in venous anastomosis. Thrombectomy is a routine treatment, an approach through a small transverse incision on graft by a 5.5 or 6 F Fogarty catheter.

Late thrombosis is the most common complication after 6 months, and mostly accompanied by venous site stenosis. Only 50–60% of grafts are patent in 2 years. The conventional practice is a hybrid procedure with Fogarty catheter and endovascular therapy. With the development of equipment, some cases can be finished totally under endovascular treatment. The different intervention methods will lead to different clinical outcomes. The present study shows that stent-graft is superior to bare-metal stent, and bare-metal stent is superior to balloon angioplasty. High-pressure balloon and cutting balloon angioplasty are better than conventional balloon, because of the significantly intimal hyperplasia in anastomosis point. Another common complication can cause graft loss is infection. The incidence is about 5–20%. Women, diabetes, repeated fistula on the same limb are the risk factors. The outcome of antibiotic treatment is not satisfactory, mostly the artificial vessels need to be removed completely.

Central Venous Catheter

The indications of CVC for dialysis in guidelines from Chinese Society of Nephrology (CSN) is described as below: ESRD patients requires dialysis immediately, but the AVF is not mature or scheduled for AVF surgery; patients with temporary catheter and no suitable vein for fistula creation; patients who have exhausted all other access options; patients with poor heart function and unable to tolerate any kinds fistula; patients who have received peritoneal dialysis, but have to stop temporarily for some reasons, and use it as a temporary method during the transition period; patients with severe system disorders or limited life expectancy.

Central venous catheters are defined as non-tunneled catheter (NTC) or non-cuffed catheter (NCC) and tunneled cuffed catheter (TCC), corresponding to the previous temporary and permanent catheter. Guidelines recommend NTC/NCC as a temporary catheter in the jugular vein that should be kept less than 4 weeks, in the femoral vein less than 1 week, and it can prolong to 2–4 weeks for ambulatory patients. If the expected dialysis is more than 4 weeks, TCC is recommended. The ultrasound is used to identify the target vein and puncture site. The procedure is performed under local anesthesia with the Seldinger technique, with the order of puncture vein is right internal jugular vein—left internal jugular vein—right femoral vein—left femoral vein. The desired catheter tip is located at 1/3 of right atrium, and the surface marker on skin is parasternal intercostal 3 and 4.

Catheter-related complications include infection, thrombosis, central vein stenosis, and fibrin sheath formation. The most common is catheter-related infections when the catheter is present for over 7 days, the probability of infection is higher in TCC than NTC/NCC, higher in femoral vein than in jugular vein. There are different degrees and severity catheter infections based on clinical findings, patients with low grade fever, occasional chills, especially during dialysis, are likely to present an intraluminal infection, and treated with antibiotics and catheter exchange using a

new exit site. Patients with symptoms and in addition a red, inflamed exit site or tender catheter tract would be removed. Another common complication of the catheter is central vein stenosis and thrombosis, directly thrombolysis or catheter thrombolysis and intervention are helpful to recover the conduit flow. Catheter-related venous stenosis is a tough problem due to the loss of the chance of fistula creation on the limb. Endovascular therapy (PTA, stenting) is the popular method to keep vessel patency.

Summary

China has a large population and a high prevalence of chronic kidney disease (CKD). The increasing incidence of hypertension, obesity, type 2 diabetes mellitus and environmental factors have exacerbated the burden and have changed the etiology of CKD in China. The creation and application of hemodialysis access indicate significant differences from region to region, but generally the current situation can be concluded that central venous catheters are more popular than AVF, which is caused by low follow-up rates and few patients having been informed about HD access in advance; however, such controllable factors can be changed through effort. Moreover, many doctors can perform dialysis, including dialysis physicians, vascular surgeons, microsurgery doctors, urologists, etc., but still there is not a uniform standard about the creation of hemodialysis access, thus leading to the heterogeneity in the quality of fistulae. A consensus reached by Chinese experts about hemodialysis access was published in 2014, aiming to establish a professional team on medical, nursing, access healthcare and management, bringing benefit for the ESRD patients.

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