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Epidemiology of hemodialysis catheter complications: survey of 865 uremic patients from 14 hemodialysis centers in Henan province of China

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Running title: Hemodialysis catheter complications in China

Abstract

Objectives: The use of catheters for hemodialysis in end-stage renal disease (ESRD) is associated with a number of complications. There is no well-established register system available for dialysis catheter in China. This study aimed to investigate the incidence rates and risk factors of catheter-related complications in different districts and populations of the Henan Province (China).

Design: Cross-sectionnal.

Setting: Fourteen hospitals of the Henan Province between January 2014 and December 2014.

Participants: 865 patients using catheters for dialysis for renal dysfunction.

Primary and secondary outcome measures: Primary outcome measures were complications, risk factors and features of the patients. Catheter-related complications included: catheter-related infection (catheter exit site infection, catheter tunnel infection, and catheter-related bacteremia infection), catheter dysfunction (thrombosis, catheter dystopy or distortion, and fibrin shell), and central vein stenosis.

Results: The overall incidence rate was 7.65/1000 catheter-day or 6.42% of placed catheters for catheter infections, 9.86/1000 catheter-day or 13.24% of placed catheters for catheter dysfunction, and 1.16/1000 catheter-day or 0.81% of placed catheters for central vein stenosis. Multivariate analysis showed that age, primary disease, education level, registered residence, payment provider, pre-established permanent vascular access, catheter type, catheter position, duration of catheter indwelling and number of indwelling surgeries were independently associated with catheter infections. Primary disease, payment provider, pre-established permanent vascular access, catheter type, catheter position, duration of catheter indwelling and

number of indwelling surgeries were independently associated with catheter dysfunction. Primary disease, pre-established permanent vascular access, catheter type, duration of catheter indwelling and number of indwelling surgeries were independently associated with central vein stenosis.

Conclusion: Rate of catheter-related complications was high in patients with ESRD in the Henan Province. Based on identified factors, strategies should be implemented to decrease complication rates.

Keywords: end-stage renal disease; hemodialysis; catheter; complication.

Article summary

Strengths and limitations of this study

- This is a large study in different settings within the same geographical region.

- Comprehensive assessment of risk factors.

- Some residual confounders were not assessed (medical therapy, nutritional status, psychosocial factors).

- The incidence of catheter-related complications could be underestimated.

Introduction

Chronic kidney disease (CKD) is defined as glomerular filtration rate (GFR) <60 ml/min/1.73 m^2 for at least 3 months, and/or signs of kidney damage for at least 3 months, as evidenced by albuminuria, urine sediment abnormalities, electrolyte abnormalities, abnormal histology, abnormal structure on imaging and/or history of kidney transplant. When CKD evolves and that renal replacement therapy is required, it is termed end-stage kidney disease (ESRD) or CKD stage 5. Dialysis should be performed when GFR reaches <15 ml/min/1.73 m^2. Vascular access for dialysis may be achieved using an arteriovenous fistula (AVF) or catheters [1]. However, the use catheter is associated with increased all-cause mortality, mainly due to catheter-related infections (CRI) [2, 3].

According to guidelines, the proportion of dialysis patients with ESRD who are using an AVF as permanent vascular access should be higher than 65% and the percentage of patients using dialysis catheter as permanent vascular access should be lower than 10% [1, 4]. However, using dialysis catheter is still very common. Indeed, according to the annual statistics of the United States Renal Data System (USRDS) [5], catheter was used in 62.6% of dialysis patients as vascular access for their first dialysis treatment in the USA, while only 16% of the patients were using AVF as vascular access for their first dialysis, and 81% of the patients were using dialysis catheter as the only vascular access or while waiting for AVF.

CRI are not the only complication that may be encountered with catheters. Indeed, complications from catheter placement, catheter replacement and/or thrombolytic instillation, clots and emboli, exit site and tunnel irritation/infection, bacteremia and sepsis may occur during catheter indwelling and after catheter removal, increasing mortality risk [6]. Indeed, CRI will happen in 2.5-5.5 per 1000 patient-days or 0.9-2.0 episodes per patient per year [7]. Catheter

clotting and thrombosis will require plasminogen activator instillations in 3.0 cases per 1000 patient-days and catheter replacement in 1.1 cases per 1000 patient-days [8]. Thrombi may encroach into the right atrium and superior vena cava, causing pulmonary embolism and superior vena cava syndrome [9]. These complications do not only threaten patients' safety and treatments' efficacy, but also waste a great amount of medical resources. Indeed, catheter low flow may result in recirculation and under-dialysis; catheter placement may result in inflammation and immune reaction; catheter use may result in anemia, requiring erythropoietin; and frequent dysfunction requires more care [6]. In 2007 alone, Medicare spendings on ESRD neared $24 billion [10], with an estimated $1.8 billion spent annually on vascular access care alone [11].

Currently, there is no well-established register system available for dialysis catheters in China that included epidemiological data about catheter-related complications, risk factors and features of the patients. Therefore, the aim of the present cross-sectional study was to investigate the incidence rates and risk factors of catheter-related complications in different districts and populations of the Henan Province (China) to help developing effective interventions and rational public health policies for the most efficient management of patients with ESRD undergoing dialysis using catheters.

Subjects and methods

Subjects

In the present cross-sectional study, 865 patients using catheters for dialysis in 14 hospitals of the Henan Province between January 2014 and December 2014 were included. The 14 hemodialysis centers were: the First Affiliated Hospital of Zhengzhou University (n=125), the

Third People's Hospital of Zhengzhou City (n=79), the Traditional Chinese Medicine Hospital of Henan Province (n=65), the Traditional Chinese Medicine Hospital of Zhengzhou city (n=36), the First Affiliated Hospital of Henan University of Science and Technology (n=66), Luoyang Eastern Hospital (n=56), Luoyang Center Hospital (n=42), Huaihe Hospital of Henan University (n=71), the First People's Hospital of Kaifeng City (n=52), the Second People's Hospital of Kaifeng City (n=47), the Puyang Oil Field General Hospital (n=49), the First People's Hospital of Xinxiang City (n=84), the Luohe Center Hospital (n=42), and the Sanmenxia Center Hospital (n=51).

The inclusion criteria for the hospitals were: 1) at least 10 hemodialysis machines in the hemodialysis center; 2) at least 50 patients receiving hemodialysis; and 3) at least 20 eligible patients. The inclusion criteria for the patients were: 1) renal dysfunction caused by any reason and receiving hemodialysis using catheters for vascular access; 2) volunteered to participate in this study, and with full capability of comprehension and communication; and 3) with complete records of previous vascular access for hemodialysis. Exclusion criteria were: 1) could not cooperate to the investigation; 2) previous medical records were not available; or 3) mental disorders or neurological diseases.

The study was approved by the ethics committee of The First Affiliated Hospital, Zhengzhou University; Institute of Nephrology, Zhengzhou University, Zhengzhou 450052, Henan Province, China. Written informed consent was obtained from each participant. Patient records/information was anonymized and de-identified prior to analysis.

Data collection

Data collected in the present study included: 1) general characteristics of the patients (age, gender, marriage, education, occupation, registered residence, provider payments, underline

disease, frequency of hemodialysis, duration of hemodialysis, and outcomes); 2) monitoring of the catheter (preparations of the vascular access before hemodialysis, reason of the first hemodialysis and the vascular access used, survival rate of non-tunnel hemodialysis catheters [NTHCs] and tunneled vascular catheters [TVCs], monitoring complications, and complications in different types of TVCs); and 3) changes in vascular accesses (times of vascular access changes and the reasons, records of the catheters used in previous hemodialysis, duration of vascular access used, and outcomes). The medical staff in the 14 participating hospitals was trained in catheter monitoring and recording of epidemiological data. Standardized questionnaires were used to record patient's information and relevant data by the investigators in each hospital. Data were managed centrally at the Henan Blood Dialysis Quality Control Center. Any discrepancy was immediately solved upon data reception. Data was registered by trained registrars.

Indwelling of the dialysis catheter

Aseptic techniques were performed in the operating room by experienced physicians from the Nephrology Department. There was no prophylactic use of antibiotics. The right internal jugular vein was chosen as the primary method for catheter indwelling, while other veins included the right external jugular vein, left internal/external jugular vein, subclavian vein, and femoral vein (according to the priority). Central vein catheterization was performed using the Seldinger technique (subcutaneous tunnel was needed for TVCs). With regard to NTHCs, single needle double-lumen catheter (Arrow International Inc., Asheboro, NC, USA) were used, and the permanent indwelling catheters included Quinton Palindrome™, Quinton Permcath™, Arrow Cannon II Plus™, and Bard HemoSplit™. The length and size of the catheters were decided according to age, height and site of catheter indwelling. Local infiltration anesthesia was chosen

as the primary anesthesia method, while general anesthesia could also be used for children or uncooperative patients. Evaluation of the patient was performed before indwelling. Doppler ultrasonography-guided puncture or venography-assisted catheter indwelling was used in patients with vascular malformation, stenosis, occlusion of the central vein or using pacemaker. Imaging examinations were performed for each patient after catheter indwelling to confirm the depth and tip position.

Hemodialysis and catheter care

Patients were dialyzed 2-4 times per week, 4-5 hours per treatment. Blood flow was 5 ml/kg per min, and the dialysate flow was 300-500 ml/min. Hollow-fiber dialyzers were selected according to the patients' body size (Fresenius®, Gambro® or Nipro® hemodialysis machines). A standard bicarbonate buffer was used as dialysate buffer. Microbiological water purity was checked monthly to ensure compliance with tight chemical and microbiological standards (<0.1 cfu/ml and <0.03 EU/ml). Hemodialysis catheters were handled only during dialysis sessions with no irrigation between treatments. According to standard nursing procedures, catheters' exit site and two ports care were cleaned with povidone iodine solution, applied with a Biopatch® (chlorhexidine-impregnated dressing), and covered with a permeable dressing at the end of each dialysis session. Each port of the catheter was filled with 5,000 U/ml of heparin solution according to the manufacturer's recommendation. Each time before opening the catheter, the exit site of the catheter was carefully observed to identify any erythema, errhysis or effusion, and the patients were asked to report any episode of fever. In addition, the temperature of each patient was measured twice during dialysis. This process was repeated strictly for each hemodialysis treatment.

Definitions of dialysis catheter-related complications [12]

Dialysis catheter-related infection

Catheter exit site infection. Definite: presence of a purulent discharge, erythema, induration or tenderness within 2 cm around the catheter exit site with a positive culture of serous discharge. Probable: presence of purulent discharge, erythema, induration, or tenderness at the catheter exit site without a positive culture of serous discharge or signs of infection from gauze or suture.

Catheter tunnel infection. Definite: presence of a purulent discharge, erythema, tenderness, and/or induration (>2 cm) along the catheter tunnel, with a positive culture of the discharge. Probable: presence of a purulent discharge, erythema, induration, tenderness along the catheter tunnel, without a positive culture result of the serous discharge or other sign of infection.

Catheter-related bacteremia infection (CRBI). Definite: same microorganism grown from at least one peripheral blood culture and from a culture of the catheter tip; or a blood culture drawn from a catheter that has a ≥3-fold greater CFU count in peripheral bold culture. Probable: positive blood cultures obtained from a catheter and/or a peripheral vein in a symptomatic patient, while no clinical evidence of infection in other organs was evident.

Catheter dysfunction

Catheter dysfunction was diagnosed if at least one of the following criteria was met: 1) peak blood flow <200 ml/min for at least 30 min; 2) mean blood flow <250 ml/min during two consecutive dialysis; or 3) inability to initiate dialysis due to inadequate blood flow even after treatments (the criteria could be lower for children or patients with low body weight).

Thrombosis. 1) Intrinsic catheter thrombosis: a thrombus is formed and attached to the internal or external surface (including the thrombi in the lumen or at the tip of the catheter). 2)

Extrinsic catheter thrombosis: thrombus caused by the presence of a catheter in the atrium, mural or central vein.

Catheter dystopy or distortion. Position of the catheter tip was at the wrong place or moved during indwelling, or the catheter distorted or folded.

Fibrin shell. Fibrin shell is a membranoid substance made up of endothelial cell, smooth muscle cells and collagen wrapped around the central venous catheter, which happened within 24 hours after catheter indwelling [12]. Fibrin shell could cause several complications including catheter dysfunction, infection, stenosis of central vein and pulmonary embolism after catheter removal.

Central vein stenosis

Damage caused by the dialysis catheter after indwelling, along with comorbidities that could induce stenosis of the central vein and thus cause obstruction syndrome, which in turn caused a series of symptoms and signs including swelling of the limbs, head and neck after stenosis of the vena cava system, and caused ulcer and infection in the limbs and encephaledema in severe cases. Clinical symptoms, Doppler ultrasound examinations and angiography were needed for diagnosis, and angiography could be used to clarify the position and range of obstruction.

Statistical analysis

SPSS 17.0 (SPSS Inc., Chicago, IL, USA) was used for the data management and analysis. General characteristics of the patients are presented as means and standard divisions or frequencies and percentages. Incidence rates per 1000 catheter-days were calculated for catheter complications. Continuous data were analyzed using the *t*-test, while categorical data were analyzed using the chi-square test. Logistic regression was used to investigate the risk factors

influencing the development of dialysis catheter related-complications, and results are presented as odds ratios (OR) and 95% confidence intervals (95%CI). Two-tailed P-values <0.05 were considered statistically significant.

Results

Characteristics of the patients

Table 1 presents the characteristics of the 865 patients included in the present study between January 2014 and December 2014, 564 being indwelled with NTHCs for 136.2±67.4 days and 385 with TVCs for 1052.3±371.3 days. Patients were aged 49.53±18.42 years. There were 495 (57.2%) males and 370 females (42.8%). Among all patients, 386 (44.6%) were receiving help from the New Rural Cooperative Medical System, 319 (36.9%) had medical insurances, and 160 (18.5%) were paying for their medical care. The three most common causes of ESRD were diabetic kidney disease (n=236, 27.3%), primary nephropathy (n=143, 16.5%) and hypertensive nephropathy (n=96, 11.1%). At the time of the study, patients had undergone dialysis for a median of 26.5 months (range: 15 days to 18 years). Hemodialysis frequency was 2/week in 375 (43.4%) patients, 3/week in 182 (21.0%), 3/2 weeks in 121 (14.0%) and 5/2 weeks in 145 (18.6%).

Complications

The overall incidence rate of catheter infection was 7.65/1000 catheter-day or 6.42% of placed catheters. The overall incidence rate of catheter dysfunction was 9.86/1000 catheter-day or 13.24% of placed catheters. The overall incidence rate of central vein stenosis was 1.16/1000 catheter-day or 0.81% of placed catheters.

Univariate analysis of factors involved in catheter-related complications

Age (OR=1.22, 95%CI:1.02-1.61, P=0.03), primary disease (OR=1.61, 95%CI: 1.14-2.13, P=0.002), education level (OR=1.38, 95%CI: 1.17-2.12, P=0.03), payment provider (OR=1.49, 95%CI: 1.05-1.59, P=0.04), pre-established permanent vascular access (OR=1.27, 95%CI: 1.01-3.13, P=0.04), catheter type (OR=2.97, 95%CI: 1.32-3.38, P=0.03), catheter position (OR=3.60, 95%CI: 2.14-5.19, P=0.006), duration of catheter indwelling (OR=3.76, 95%CI=1.63-4.41, P=0.005) and number of indwelling surgeries (OR=2.19, 95%CI: 1.66-4.66, P=0.03) were associated with CRI (Table 2).

Age (OR=1.19, 95%CI:1.02-1.92, P=0.04), primary disease (OR=1.42, 95%CI: 1.237-1.842, P=0.03), payment provider (OR=1.89, 95%CI: 1.13-4.38, P=0.04), frequency of dialysis (OR=2.14, 95%CI: 1.13-3.73, P=0.03), age at first dialysis (OR=3.24, 95%CI: 1.32-4.33, P=0.04), pre-established permanent vascular access (OR=1.35, 95%CI:1.14-1.98, P=0.02), catheter type (OR=2.16, 95%CI: 1.24-4.19, P=0.02), catheter position (OR=3.54, 95%CI: 1.27-4.14, P=0.01), duration of catheter indwelling (OR=2.31, 95%CI=1.33-3.22, P=0.04) and number of indwelling surgeries (OR=3.00, 95%CI: 2.14-5.42, P=0.04) were associated with catheter dysfunction (Table 2).

Primary disease (OR=2.13, 95%CI: 1.65-2.43, P=0.02),pre-established permanent vascular access (OR=2.17, 95%CI: 1.37-3.93, P=0.03), catheter type (OR=2.93, 95%CI: 1.38-3.83, P=0.02), catheter position (OR=1.83, 95%CI: 1.13-3.37, P=0.05), duration of catheter indwelling (OR=1.55, 95%CI:1.24-2.12, P=0.01) and number of indwelling surgeries (OR=2.85, 95%CI: 1.13-3.97, P=0.03) were associated with central vein stenosis (Table 2).

Multivariate analysis of factors involved in catheter-related complications

Age (OR=1.83, 95%CI:1.15-2.61, P=0.03), primary disease (OR=1.52, 95%CI: 1.21-2.22, P=0.03), education level (OR=1.68, 95%CI: 1.06-1.42, P=0.04), registered residence (OR=1.47, 95%CI: 1.48-2.35, P=0.03), payment provider (OR=1.41, 95%CI: 1.04-1.98, P=0.04), pre-established permanent vascular access (OR=2.65, 95%CI: 2.13-2.51, P=0.01), catheter type (OR=1.79, 95%CI: 1.50-2.44, P=0.04), catheter position (OR=3.07, 95%CI: 2.54-5.48, P=0.008), duration of catheter indwelling (OR=2.56, 95%CI=1.62-3.52, P=0.04) and number of indwelling surgeries (OR=2.14, 95%CI: 1.43-4.66, P=0.02) were independently associated with CRI (Table 3).

Primary disease (OR=1.64, 95%CI:1.341-1.841, P=0.03), payment provider (OR=1.76, 95%CI: 1.26-3.67, P=0.04), pre-established permanent vascular access (OR=3.40, 95%CI: 1.54-4.65, P=0.03), catheter type (OR=1.47, 95%CI:1.35-1.76, P=0.04), catheter position (OR=1.20, 95%CI: 1.11-1.85, P=0.04), duration of catheter indwelling (OR=3.02, 95%CI=1.33-3.22, P=0.01) and number of indwelling surgeries (OR=3.71, 95%CI: 1.42-5.86, P=0.008) were independently associated with catheter dysfunction (Table 3).

Primary disease (OR=2.64, 95%CI: 1.25-2.83, P=0.02), pre-established permanent vascular access (OR=1.44, 95%CI: 1.15-2.01, P=0.03), catheter type (OR=1.52, 95%CI: 1.28-2.17, P=0.03), duration of catheter indwelling (OR=3.25, 95%CI=2.65-4.73, P=0.02) and number of indwelling surgeries (OR=3.41, 95%CI: 1.83-4.25, P=0.002) were independently associated with central vein stenosis (Table 3).

Complications according to the type of temporary venous catheter

Table 4 shows the incidence of complications from different types of TVCs. The incidence rates of infection and fibrin shell during the use of the four types of TVCs were not significantly different (P>0.05). However, the incidence rate of thrombosis was significantly higher in patients

using HemoSplit™ catheters compared with other TVCs (P<0.05), and the incidence rate was the lowest in the ones using Palindrome™ catheters (P<0.05). The incidence rate of dystopy or distortion in patients using Permcath™ or Palindrome™ catheters was higher compared with Cannon® II Plus™ or HemoSplit™ catheters (P<0.05). The incidence rate of central vein stenosis was lower in patients using Cannon® II Plus™ catheters compared with other catheters (P<0.05). The Kt/V value was higher in patients using Palindrome™ catheters compared with the other types of TVCs, but the difference was not statistically significant.

Complications according to the type of catheter

Compared with TVCs, Table 5 shows that the incidence of catheter exit site infections was higher with NTHCs, the incidence of catheter-related bloodstream infection was lower, the incidence of catheter thrombosis was higher, the incidence of distortion was higher, and the incidence of central vein stenosis was lower.

Discussion

The objective of the present study was to investigate the incidence rates and risk factors of catheter-related complications in different districts and populations of the Henan Province (China). Results showed that the overall incidence rate was 7.65/1000 catheter-day or 6.42% of placed catheters for catheter infections, 9.86/1000 catheter-day or 13.24% of placed catheters for catheter dysfunction, and 1.16/1000 catheter-day or 0.81% of placed catheters for central vein stenosis. Multivariate analysis showed that age, primary disease, education level, registered residence, payment provider, pre-established permanent vascular access, catheter type, catheter position, duration of catheter indwelling and number of indwelling surgeries were independently

associated with. Primary disease, payment provider, pre-established permanent vascular access, catheter type, catheter position, duration of catheter indwelling and number of indwelling surgeries were independently associated with catheter dysfunction. Primary disease, pre-established permanent vascular access, catheter type, duration of catheter indwelling and number of indwelling surgeries were independently associated with central vein stenosis.

Previous studies showed that the rate of CRI is about 3.8-6.5 per 1000 catheter-day [13, 14]. However, the rate of CRI was higher in the present study. We found that the overall rate of catheter infection was 7.65/1000 catheter-day or 6.42% of placed catheters for all patients, 6.85/1000 catheter-day or 5.72% of placed TVCs, and 8.82/1000 catheter-day or 7.55% of placed NTHCs. Some reasons might be responsible for this higher rate. The first is patient factors. Indeed, age of the patients included in the present study was relatively high (mean age: 49.53±18.42 years); 60.9% of the patients were ages >45 years, and the oldest patient was 92 years old. Advanced age is generally associated with multiple organ function damage, malnutrition, impaired immunity and feebleness, all of which could increase the risk of catheter infection. The most frequent primary disease was diabetes (27.3%), and long-term diabetes is associated with peripheral vascular disorders, preventing AVF surgery and requiring the use of catheters for dialysis. In addition, Saxena et al. [15] reported that the risk of CRI was increased by 60% in patients with diabetes. Patients with higher education or ability of communication could better understand the severity of their disease and acquire the knowledge about self-care of dialysis catheters. Patients living in cities generally possess higher educational level than the ones living in rural areas; however, most of the patients included in the present study were from rural areas (57.5%) or with an education level of middle school or lower. Dialysis represents a heavy financial burden. In the present study, most of the patients were with the medical

insurance of the New Rural Cooperative Medical System (44.6%) or even had no medical insurance (18.5%).

Risk factors for CRI included no pre-established permanent vascular access, type of catheter, position of catheter indwelling, duration of catheter indwelling, and number of indwelling surgeries. The overall infection rate in the NTHCs group was significantly higher than in the TVCs group, which is supported by previous findings [14]. Indeed, the longer indwelling time might have been the main reason causing the higher rate of CRBI in the TVCs group (1052.28±371.26 days) than in the NTHCs group (136.2±67.4 days). Oliver et al. [14] showed that the duration of catheter indwelling was a high risk factor of CRI. Weijmer et al. [16] suggested that for patients needing NTHCs for more than 2 weeks, the catheter should be changed to TVCs to reduce the risk of infection. Longer catheter indwelling time is generally associated with low educational level of the patients (they were not fully aware of the severity of the disease). In the present study, 85.5% of the patients experienced two or more surgeries for vascular access.

Catheter dysfunction is characterized by poor blood flow. There is then a need for adjustments of the position, reverse connection of arteriovenous catheter, or thrombolytic therapy. This dysfunction is mainly caused by mechanical factors including thrombosis, fibrin shell, catheter dystopy, or distortion. Embolism can also been found in the catheter, attached to the catheter wall to form mural thrombi, and further form a fibrin shell around the tip of the catheter. Previous studies showed that 98% of catheter dysfunctions occurring within 2 weeks were caused by catheter embolism or fibrin shell [4]. Suhocki et al. [17] reported that among 163 patients with catheter dysfunctions, 74.2% were with catheter embolism and 23.3% were with fibrin shell. Napalkov et al. [18] performed an investigation in 3213 patients using dialysis catheters and found that the incidence of thrombosis was 8.6/1000 catheter-day. In the present study, the overall

incidence rate of catheter dysfunction was 9.86/1000 catheter-day for all patients, 8.64/1000 catheter-day for placed TVCs (which was in accordance with previous studies) and 12.86/1000 catheter-day for placed NTHCs (which was substantially higher than the previous studies). This high incidence could be associated with the prolonged duration of NTHCs indwelling or increased number of indwelling surgeries. In the present study, a great proportion of patients (38.4%) were aged patients with hypertension or diabetes. Hyperlipidemia, arteriosclerosis, hematonosis and cancers can induce hypercoagulability [19]. In addition, patients with uremia generally have high homocysteine levels and microinflammation, which can increase thrombogenesis [19]. A too high number of indwelling surgeries could damage the vascular wall, and the exposure of endothelium could promote platelet adhesion and activate endogenous coagulation pathway, which could be further aggravated by the local disturbance of hemodynamics after catheter indwelling [20].

Fibrin shell may occur in all sorts of central venous catheters, which not only induce catheter dysfunction, but also induce a series of complications including infection, thrombogenesis, catheter removal and pulmonary embolism [21, 22]. Previous studies showed that the incidence of fibrin shell was generally high. In a study performed by Oliver et al. [23], 70% of the patients with indwelled catheters were with fibrin shell. Schon et al. [24] also showed that 38% of the patients with catheter dysfunction had a fibrin shell. In the present study, the incidence rate of fibrin shell was greatly lower than in previous studies, which was 3.69/1000 catheter or 2.18% of placed catheters for the patients in the NTHCs group and 3.81/1000 catheter-day or 2.41% of placed catheters for the ones in the TVCs group. Although treating with drugs or fibrin dissection could restore partial catheter function in some cases, there are some disadvantages including the high recurrence rate after drug-therapy and the high price of fibrin dissection. Therefore, although

several clinicians speculated that catheter dysfunction could be associated with the formation of fibrin shell, the medical cost pushed them to changing dialysis catheter instead of performing further imaging examinations, which decreased the diagnostic rate of fibrin shell.

In the present study, long-term indwelling of catheter was an important risk factors of central vein stenosis in dialysis patients. Previous studies showed that the incidence rate of central vein stenosis could be as high as 25%-40% [25]. Several studies also showed that 95% of the patients with central vein stenosis had a history of catheter indwelling, while only 13.6% of the patients without history of catheter indwelling developed central vein stenosis. However, repeated indwelling surgeries could increase the incidence rate of central vein stenosis in dialysis patients by 3-fold [26]. After catheter indwelling, mechanical injuries to the vascular endothelium, secondary activation of platelet and coagulation pathways, changes in hemodynamics and extrinsic compression of catheter-surrounding tissues participate in the development of central vein stenosis [27]. Angiography is the gold standard for the diagnosis of central vein stenosis [28]. In the present study, the overall incidence rate of central vein stenosis (1.16/1000 catheter-day or 0.81% of placed catheters) was relatively low, which could be caused by the low diagnostic rate of central vein stenosis. Indeed, only patients with severe symptoms (including severe facial swelling, limb swelling, limb pain, and intracranial hypertension) were examined by angiography, while most patients without symptom or only with mild symptoms were not diagnosed due to the high medical costs or insufficient awareness from the clinicians. The incidence rate was significantly higher in patients using TVCs (1.35/1000 catheter-day or 0.81% of placed catheters) compared with NTHCs (0.35/1000 catheter-day or 0.07% of placed catheters, $P<0.05$), which might be associated with the stimulations to the vascular wall caused by the long duration of TVCs indwelling. Diabetes is an important risk factor of central vein stenosis, which could be

caused by the facts that diabetic patients receiving dialysis were affected by long-term influences of high glucose, chronic inflammation, and lipid metabolism disorders, increasing the risk of angiosclerosis, vascular wall thickening, reduced elasticity, thrombogenesis and stenosis [29].

In this study, four different types of TVCs were used in the 14 participating hospitals. Since no specific coating was applied to each of the four types of TVCs to prevent infection and thrombosis, and since the indwelling duration of these four types of TVCs was similar, no significant difference in the incidence rate of catheter infection or central vein stenosis was found among these 4four types of TVCs. However, the incidence of catheter embolism was significantly higher with the HemoSplit™ catheter compared with the other types, and the incidence of catheter embolism in patients using the Palindrome™ catheter was the lowest, which could be associated with different designs of the side holes at the tip of the catheters. The side holes in Palindrome™ catheter are relatively large rectangle laser notching, which is relatively difficult to be adhered by thrombi [30], while the side holes in the HemoSplit™ catheter are relatively small round holes that could be easily adhered by thrombi. The texture and cuff ring are identical in the Palindrome™ and Permcath™ catheters, of which the rates of dystopy and distortion were significantly higher compared with the other two types of TVCs. The specific "retrograde design" of the Cannon II Plus catheter [31] make sure that the cuff ring is fixed to the clavicle, while the cuff ring in the HemoSplit™ catheter can be closely connected with the adjacent tissues. Therefore, these two catheters had a lower risk of dystopy and distortion. The incidence rate of central vein stenosis with the Cannon II Plus™ catheter was the lowest among all the four types of TVCs, which could be associated with the facts that the tip of the catheter was placed in the right atrium and the stimulation to the superior vena cava was relatively small.

This present study has several limitations. First, there remains residual confounding from unmeasured variables such as medical therapy, nutritional status of the patients, biochemical indexes and psychosocial factors. Second, the Henan Province covers a large area and has a large population, and the levels of economics, culture and healthcare varies greatly among different districts. Since all 14 participating hospitals included were from the districts with relatively high economic level, the epidemiological features of catheter-related complications could be different from remote areas or other districts with relatively low economic level. Therefore, the incidence of catheter-related complications could be underestimated in the present study.

In conclusion, patients receiving dialysis in the Henan Province have a high rate of dialysis catheter use with long duration of temporary catheter indwelling, which resulted in a high incidence of catheter-related complications. Therefore, health administration need to develop policies about establishing vascular access as soon as possible.

Authors' contributions

KW and ZSL have made substantial contributions to conception and design; KW, PW, XHL, XQL and ZSL have made substantial contributions to acquisition of data, or analysis and interpretation of data; KW and ZSL has been involved in drafting the manuscript or revising it critically for important intellectual content; all authors have given final approval of the version to be published.

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Competing interests

The authors declare that they have no competing interests.

Data sharing statement

Technical appendix, statistical code and dataset are available from the corresponding author at the Dryad repository, which will provide a permanent, citable and open access repository for the dataset.

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Table 1. Patient characteristics

Characteristics	**Values** (N=865)
NTHCs	564
TVCs	385
Indwelling time (days)	
NTHCs	136.2±67.4
TVCs	1052.3±371.3
Permanent catheter	
Quinton Palindrome™	103 (24.4%)
Quinton Permcath™	91 (21.6%)
Arrow Cannon II Plus™	101 (29.1%)
Bard HemoSplit™	90 (24.9%)
Age	49.53±18.42
≤18	126 (14.6%)
19-44	212 (24.5%)
45-59	236 (27.3%)
≥60	291 (33.6%)
Gender	
Male	495 (57.2%)
Female	370 (42.8%)
Marital status	
Married	487 (56.3%)
Single	285 (32.9%)

Widowed or divorced	93 (10.8%)
Education	
University	152 (17.6%)
Middle school	481 (55.6%)
Below primary school	232 (26.8%)
Occupation	
Farmer	352 (40.7%)
Worked	124 (14.3%)
Office worker	95 (11.0%)
Retired	165 (19.1%)
Unemployed	129 (14.9%)
Registered residence	
Rural	497 (57.5%)
Urban	368 (42.5%)
Medical costs	
New Rural Cooperative Medical System	386 (44.6%)
Medical insurance	319 (36.9%)
Self-paying	160 (18.5%)
Primary disease	
Diabetic kidney disease	236 (27.3%)
Primary nephropathy	143 (16.5%)
Hypertensive nephropathy	96 (11.1%)
Acute renal failure	44 (5.1%)

Obstructive nephropathy	72 (8.3%)
Renal tubular interstitial disease	62 (7.2%)
Drug-induced renal damage	39 (4.5%)
Myeloma	24 (2.8%)
Others	103 (11.9%)
Hemodialysis duration, median (range)	26.5 months (15 day-18 years)
Hemodialysis frequency	
2/week	375 (43.4%)
3/week	182 (21.0%)
3/2 weeks	121 (14.0%)
5/2 weeks	145 (16.8%)

Table 2. Univariate logistic regression of factors influencing the development of dialysis catheter-related complications

Variables	Catheter-infection			Catheter dysfunction			Central vein stenosis		
	OR	P	95%CI	OR	P	95%CI	OR	P	95%CI
Age	1.215	0.026	1.018-1.613	1.194	0.041	1.017-1.918	2.312	0.715	0.926-2.726
Gender	1.259	0.128	0.719-1.313	1.528	0.613	0.863-2.017	1.791	0.541	0.396-2.058
Primary disease	1.612	0.002	1.142-2.129	1.421	0.034	1.237-1.842	2.129	0.017	1.651-2.431
Marriage	1.229	0.270	0.428-1.679	1.741	0.415	0.693-2.315	1.391	0.569	0.814-2.381
Education	1.381	0.029	1.168-2.124	0.941	0.761	0.719-1.815	1.724	0.481	0.739-1.819
Occupation	1.004	0.986	0.872-1.543	1.953	0.631	0.815-1.926	1.317	0.519	0.681-2.281
Registered residence	1.612	0.038	1.476-2.139	1.831	0.841	0.561-1.849	1.429	0.732	0.548-1.619
Payment provider	1.491	0.041	1.049-1.591	1.891	0.039	1.128-4.380	1.281	0.514	0.471-1.519
Frequency of dialysis	2.693	0.438	1.731-3.259	2.138	0.028	1.129-3.726	0.663	0.157	0.251-1.463
Age at first dialysis	3.596	0.439	2.148-8.168	3.241	0.035	1.316-4.329	0.928	0.491	0.318-1.512

Pre-established permanent vascular access	1.267	0.039	1.014-3.127	1.347	0.015	1.136-1.982	2.172	0.031	1.367-3.931
Catheter type	2.967	0.025	1.316-3.384	2.156	0.017	1.239-4.185	2.931	0.021	1.381-3.829
Catheter position	3.596	0.006	2.137-5.189	3.538	0.014	1.269-4.143	1.831	0.046	1.126-3.371
Duration of catheter indwelling	3.763	0.005	1.631-4.413	2.314	0.038	1.329-3.219	1.548	0.014	1.235-2.123
Number of indwelling surgeries	2.192	0.029	1.661-4.661	3.004	0.041	2.137-5.421	2.849	0.003	1.128-3.971

Table 3. Multivariate logistic regression of the factors influencing dialysis catheter-related complications

Variable	Catheter-infection			Catheter dysfunction			Central vein stenosis		
	OR	P	95%CI	OR	P	95%CI	OR	P	95%CI
Age	1.83	0.031	1.148-2.613	-	-	-	-	-	-
Primary disease	1.517	0.029	1.214-2.215	1.641	0.029	1.341-1.841	2.639	0.016	1.245-2.826
Educational level	1.681	0.037	1.062-1.415	-	-	-	-	-	-
Registered residence	1.471	0.029	1.476-2.351	-	-	-	-	-	-
Payments provider	1.414	0.035	1.041-1.981	1.762	0.041	1.261-3.671	-	-	-
Pre-establishment of permanent vascular access	2.651	0.012	2.132-2.513	3.402	0.027	1.541-4.651	1.437	0.028	1.152-2.014
Type of catheter	1.787	0.043	1.496-2.438	1.472	0.041	1.352-1.762	1.515	0.031	1.281-2.171
Position of catheter indwelling	3.069	0.008	2.539-5.482	1.204	0.038	1.106-1.852	-	-	-
Duration of catheter	2.564	0.041	1.617-3.519	3.017	0.012	1.329-3.219	3.251	0.015	2.651-4.726

indwelling									
Number of indwelling surgeries	2.138	0.021	1.428-4.661	3.706	0.008	1.417-5.862	3.412	0.002	1.829-4.251

Table 4. Complications of hemodialysis catheters by TVC design type

Complications			TVC			
			Palindrome™ (103 patient-time)	Permcath™ (91 patient-time)	Cannon II Plus™ (101 patient-time)	HemoSplit™ (90 patient-time)
Infection	Catheter exit site infection	(100%)	5.46	5.41	5.49	5.47
		/1000 catheter-day	6.92	6.89	6.96	6.94
	Catheter tunnel infection	(100%)	1.62	1.59	1.61	1.64
		/1000 catheter-day	2.71	2.69	2.70	2.73
	CRBSI	(100%)	4.84	4.82	4.79	4.81
		/1000 catheter-day	6.63	6.65	6.59	6.67
Catheter dysfunction	Thrombosis	(100%)	9.81	11.61	11.79	12.95
		/1000 catheter-day	6.31	8.17	8.31	9.82
	Fibrin shell	(100%)	3.85	3.92	2.72	3.06

	/1000 catheter-day	4.85	4.96	3.12	3.34
	(100%)	1.96	1.71	0.93	0.82
Dystopy or distortion	/1000 catheter-day	2.93	2.97	1.67	1.73
	(100%)	1.13	1.15	0.59	1.11
Central vein stenosis	/1000 catheter-day	3.21	3.14	2.15	3.19
Kt/V		1.42±0.12	1.28±0.37	1.31±0.25	1.36±0.36

Table 5. Incidence of hemodialysis catheter complications

Complication			TVCs					NTHCs		
			RIJV (203)	LIJV (87)	EJV (65)	FV (19)	SV (11)	RIJV (312)	LIJV (169)	FV (83)
Catheter infection	Catheter exit site infection	(100%)	5.37	5.39	5.35	6.91	5.33	7.39	7.42	8.23
		/1000 catheter-day	6.23	6.45	6.27	7.03	6.16	8.76	9.03	9.65
	Catheter tunnel infection	(100%)	1.59	1.61	1.63	1.89	1.65	/	/	/
		/1000 catheter-day	2.67	2.69	2.75	3.52	2.71	/	/	/
	Catheter-related blood stream	(100%)	4.32	4.34	4.36	6.73	4.31	2.67	2.71	2.55
		/1000	6.07	5.89	5.93	7.12	5.85	4.98	5.05	4.93

	infection (CRBSI)	catheter-day (100%)	11.22	11.87	11.20	14.21	11.25	18.65	18.79	20.33
	Thrombosis	/1000 catheter-day (100%)	8.46	8.49	8.43	8.89	8.47	12.93	12.98	16.97
Catheter dysfunction	Fibrin shell	/1000 catheter-day (100%)	2.39	2.43	2.36	2.59	6.43	2.15	2.18	2.19
	Dystopy or distortion	/1000 catheter-day (100%)	3.76	4.34	3.75	4.89	3.80	3.67	3.71	4.71
			1.13	1.38	1.10	1.52	1.20	3.31	3.35	3.89
			2.14	2.15	2.10	3.22	2.19	4.38	4.41	5.16
Stenosis of central vein			1.21	1.83	1.22	0	1.26	0.44	0.49	0

/1000								
catheter-day	3.56	3.12	3.58	0	3.60	1.50	1.54	0

RIJV: right internal jugular vein; LIJV: left internal jugular vein; FV: femoral vein; EJV: external jugular vein; SV: subclavian vein

Notes: 1) As only very limited patients were using TVCs in the left external jugular vein, and no patient was using NTHCs in external jugular vein or subclavian vein, no statistical analysis was performed for these patients. 2) Imaging examinations were needed to confirm fibrin shell and central vein stenosis before the patients were included in the statistical analyses.

STARD checklist for reporting of studies of diagnostic accuracy

(version January 2003)

Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	N/A
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	N/A
METHODS			
Participants	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	6-7
	4	Participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	6-7
	5	Participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in item 3 and 4? If not, specify how participants were further selected.	6-7
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	N/A
Test methods	7	The reference standard and its rationale.	N/A
	8	Technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	9-10
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	N/A
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	N/A
	11	Whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	N/A
Statistical methods	12	Methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	N/A
	13	Methods for calculating test reproducibility, if done.	N/A
RESULTS			
Participants	14	When study was performed, including beginning and end dates of recruitment.	12
	15	Clinical and demographic characteristics of the study population (at least information on age, gender, spectrum of presenting symptoms).	12
	16	The number of participants satisfying the criteria for inclusion who did or did not undergo the index tests and/or the reference standard; describe why participants failed to undergo either test (a flow diagram is strongly recommended).	N/A
Test results	17	Time-interval between the index tests and the reference standard, and any treatment administered in between.	N/A
	18	Distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	N/A
	19	A cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	N/A
	20	Any adverse events from performing the index tests or the reference standard.	N/A
Estimates	21	Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	N/A
	22	How indeterminate results, missing data and outliers of the index tests were handled.	N/A
	23	Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	N/A
	24	Estimates of test reproducibility, if done.	N/A
DISCUSSION	25	Discuss the clinical applicability of the study findings.	15-21

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Epidemiology of hemodialysis catheter complications: survey of 865 uremic patients from 14 hemodialysis centers in Henan province of China

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Epidemiology of hemodialysis catheter complications: survey of 865 uremic patients from 14 hemodialysis centers in Henan province of China

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Running title: Hemodialysis catheter complications in China

Abstract

Objectives: The use of catheters for hemodialysis in end-stage renal disease (ESRD) is associated with a number of complications. There is no well-established register system available for dialysis catheters in China. This study aimed to investigate the incidence rates and risk factors of catheter-related complications in different districts and populations of Henan Province (China).

Design: Cross-sectional.

Setting: Fourteen hospitals of Henan Province between October 2013 and October 2014.

Participants: 865 patients with renal dysfunctions using catheters for dialysis.

Main outcome measures: Main outcome measures were complications, risk factors and features of the patients. Catheter-related complications included: catheter-related infection (catheter exit site infection, catheter tunnel infection, and catheter-related bloodstream infection), catheter dysfunction (thrombosis, catheter malposition or kinking, and fibrin shell formation), and central vein stenosis.

Results: The overall incidence rate was 7.74/1000 catheter-day or 38.61% of all patients for catheter infections, 10.58/1000 catheter-day or 56.65% of all patients for catheter dysfunction, and 0.68/1000 catheter-day or 8.79% of all patients for central vein stenosis. Multivariate analysis showed that age, primary disease, education level, registered residence, nephropathy visit before dialysis and pre-established permanent vascular access, oral drugs for preventing catheter thrombus, serum albumin levels, and ferritin levels were independently associated with catheter infections. Registered residence, oral drugs for preventing thrombus, imaging examination after catheter indwelling, catheter type, medical insurance, nephropathy visit before

dialysis and pre-established permanent vascular access, catheter position, approach vessels and hemoglobin level were independently associated with catheter dysfunction. Primary disease, nephropathy visit before dialysis and pre-established permanent vascular access, oral drugs for preventing catheter thrombus, catheter location and number of indwelling surgeries, were independently associated with central vein stenosis.

Conclusion: The rate of catheter-related complications was high in patients with ESRD in Henan Province. Based on identified factors, strategies should be implemented to decrease complication rates.

Keywords: end-stage renal disease; hemodialysis; catheter; complication.

Article summary

Strengths and limitations of this study

- This is a large study in different settings within the same geographical region.

- Comprehensive assessment of risk factors.

- Some residual confounders were not assessed (medical therapy, nutritional status, psychosocial factors).

- The incidence of catheter-related complications could be underestimated.

Introduction

Dialysis for end-stage kidney disease (ESRD) may be achieved using an arteriovenous fistula (AVF) or catheters [1]. However, the use of catheter is associated with increased all-cause mortality, mainly due to catheter-related infections (CRI) [2, 3]. According to guidelines, the proportion of patients with ESRD on dialysis who are using an AVF as permanent vascular access should be higher than 65% and the percentage of patients using dialysis catheter as permanent vascular access should be lower than 10% [1, 4]. However, using dialysis catheter is still very common. Indeed, according to the annual statistics of the United States Renal Data System (USRDS) [5], catheter was used in 62.6% of dialysis patients as vascular access for their first dialysis treatment in the USA, while only 16% of the patients were using AVF as vascular access for their first dialysis, and 81% of the patients were using dialysis catheter as the only vascular access or while waiting for the maturation of an AVF.

In addition to CRI, complications from catheter placement, catheter replacement and/or thrombolytic therapy, clots and emboli, exit site and tunnel irritation/infection, bacteremia and sepsis may all occur during catheter indwelling and after catheter removal, increasing mortality risk [6]. Indeed, CRI will happen in 2.5-5.5 patients per 1000 patient-days or 0.9-2.0 episodes per patient per year [7]. Catheter clotting and thrombosis will require plasminogen activator instillations in 3.0 cases per 1000 patient-days and catheter replacement in 1.1 cases per 1000 patient-days [8]. Thrombi may encroach into the right atrium and superior vena cava, causing pulmonary embolism and superior vena cava syndrome [9]. These complications not only threaten patients' safety and treatments' efficacy, but also waste medical resources. Catheter low flow may result in recirculation and under-dialysis; catheter placement may result in inflammation and immune reaction; catheter use may result in anemia, requiring erythropoietin; and frequent

dysfunction requires more care [6]. In 2007 alone, Medicare spending on ESRD neared $24 billion [10], with an estimated $1.8 billion spent annually on vascular access care [11].

Currently, there is no well-established register of dialysis catheters in China that reveals epidemiological data about catheter-related complications, risk factors and features of the patients. Therefore, the aim of the present cross-sectional study was to investigate the incidence rates and risk factors of catheter-related complications in different districts and populations of Henan Province (China) to help develop effective interventions and rational public health policies for the most efficient management of patients with ESRD undergoing dialysis using catheters.

Subjects and methods

Subjects

In the present cross-sectional study, 865 patients using catheters for dialysis in 14 hospitals of Henan Province between October 2013 and October 2014 were prospectively included. The 14 hemodialysis centers were: the First Affiliated Hospital of Zhengzhou University (n=125), the Third People's Hospital of Zhengzhou City (n=79), the Traditional Chinese Medicine Hospital of Henan Province (n=65), the Traditional Chinese Medicine Hospital of Zhengzhou city (n=36), the First Affiliated Hospital of Henan University of Science and Technology (n=66), Luoyang Eastern Hospital (n=56), Luoyang Center Hospital (n=42), Huaihe Hospital of Henan University (n=71), the First People's Hospital of Kaifeng City (n=52), the Second People's Hospital of Kaifeng City (n=47), the Puyang Oil Field General Hospital (n=49), the First People's Hospital of Xinxiang City (n=84), the Luohe Center Hospital (n=42), and the Sanmenxia Center Hospital

(n=51).

The inclusion criteria for the hospitals were: 1) at least 10 hemodialysis machines in the hemodialysis center; 2) at least 50 patients undergoing hemodialysis; and 3) at least 20 patients eligible for the study. The inclusion criteria for the patients were: 1) renal dysfunction caused by all sorts of reasons and undergoing hemodialysis using catheters for vascular access; 2) willingness to participate in the study, and with full capability of comprehension and communication; and 3) with complete records of previous vascular access for hemodialysis. Exclusion criteria were: 1) could not cooperate to the investigation; 2) previous medical records were not available; 3) <18 years of age or 4) with severe mental disorders or neurological diseases.

The study was approved by the ethics committee of the First Affiliated Hospital, Zhengzhou University. Written informed consent was obtained from each participant. Patient records/information was anonymized and de-identified prior to analysis.

Data collection

Data collected in the present study included: 1) general characteristics of the patients (age, gender, marriage, education, occupation, registered residence, provider payments, underlying disease, frequency of hemodialysis, duration of hemodialysis, and outcomes); 2) monitoring of the catheter (preparations of the vascular access before hemodialysis, reason for the first hemodialysis and the vascular access used, survival rates of non-tunnel hemodialysis catheters [NTHCs] and tunneled vascular catheters [TVCs], monitoring complications, and complications in different types of catheter); and 3) changes in vascular accesses (frequencies of vascular access changes and related reasons, records of catheters used in previous hemodialysis, duration of vascular access, and outcomes). The medical staff in the 14 participating hospitals was trained

in catheter monitoring and recording of epidemiological data. Standardized questionnaires were used to record patient's information and relevant data by the investigators in each hospital. Data were managed centrally at the Henan Blood Dialysis Quality Control Center. Any discrepancy was immediately solved upon data reception. Data was registered by trained registrars.

Indwelling of dialysis catheter

Aseptic practices were performed in the operating room by experienced physicians (the attending specialist in kidney diseases with a minimum of 1 year experience and 100 cases of catheter placement) from the Nephrology Department. The venipuncture site was prepared by disinfection with alcohol lipid-removal for 3 times, then by betadine (a common disinfector used in all 14 hospitals). There was no prophylactic use of antibiotics. The first choice for catheter placement was the right internal jugular vein, while other choices included the right external jugular vein, left internal/external jugular vein, subclavian vein, and femoral vein (according to the priority). Central vein catheterization was performed using the Seldinger technique (subcutaneous tunnel was needed for TVCs). With regard to NTHCs, single needle double-lumen catheters (ARROW: Arrow International Inc., Asheboro, NC, USA; DIALL: DIALL Medical Technology Co., Ltd. Zhengzhou, CHINA; ABLE: Guangdong Baihe Medical Technology Co., Ltd. Foshan，CHINA; TYCO：Covidien Co., Ltd. USA) were used, and the permanent indwelling catheters were placed with Quinton Palindrome™ (Covidien Co., Ltd. USA), Quinton Permcath™ (Covidien Co., Ltd. USA), Arrow Cannon II Plus™ (Arrow International Inc., Asheboro, NC, USA), and Bard HemoSplit™ (C. R. Bard, Inc.USA). The length and size of catheters were decided according to age, height and site of catheter indwelling. The type of catheter was decided by the hospital. Local infiltration anesthesia was chosen as the primary anesthesia method, while general anesthesia could also be used for children or uncooperative

patients. Evaluation of the patient was performed before indwelling. Doppler ultrasonography-guided puncture or venography-assisted catheter indwelling was used in patients with vascular malformation, stenosis, and occlusion of the central vein or using pacemaker.

Hemodialysis and catheter care

Patients were dialyzed 2-4 times per week, 4-5 hours per treatment. Blood flow was 5 ml/kg per min, and the dialysate flow was 300-500 ml/min. Hollow-fiber dialyzers were selected according to the patients' body size (Fresenius®, Gambro® or Nipro® hemodialysis machines). A standard bicarbonate buffer was used as dialysate buffer. Microbiological water purity was checked monthly to ensure compliance with tight chemical and microbiological standards (<0.1 cfu/ml and <0.03 EU/ml). Hemodialysis catheters were handled only during dialysis sessions with no irrigation between treatments. According to standard nursing procedures, the catheters' exit site and two ports care were cleaned with povidone iodine solution, applied with a Biopatch® (chlorhexidine-impregnated dressing), and covered with a permeable dressing at the end of each dialysis session. Each port of the catheter was filled with 5,000 U/ml of heparin solution according to the manufacturer's recommendation. Each time before opening the catheter, the exit site of the catheter was carefully checked for any redness, swelling, bleeding or exudate, and the patients were asked to report any episode of fever. In addition, the temperature of each patient was measured twice during dialysis. This process was repeated strictly for each hemodialysis treatment.

Definitions of dialysis catheter-related complications [12]

Dialysis catheter-related infection

Catheter exit site infection. Diagnosed: presence of pus, redness, induration, or tenderness within 2 cm around the catheter exit site, pus secretion culture was positive. Suspicious: presence of pus, redness, induration, or tenderness at the catheter exit site, yet pus secretion culture was negative. No signs of infection in gauze or sutures.

Catheter tunnel infection. Diagnosed: presence of pus, redness, tenderness, and/or induration (>2 cm) along the catheter tunnel, with a positive bacteria culture from secretions. Suspicious: presence of pus, redness, induration, and tenderness along the catheter tunnel, without a positive culture from secretions or infections in other loci.

Catheter-related bacteremia infection (CRBI). Diagnosed: the same microorganism grown from peripheral blood culture and catheter tip culture for at least once; or the count of colonies cultured from catheter lock solution is ⩾3-fold than the count from peripheral blood culture. Suspicious: positive blood cultures obtained from catheter lock solution and/or peripheral blood in a symptomatic patient, while no clinical evidence of infections in other loci.

Catheter dysfunction

Catheter dysfunction was diagnosed when at least one of the following criteria was met: 1) peak blood flow <200 ml/min for at least 30 min; 2) mean blood flow <250 ml/min during two consecutive dialysis; or 3) unable to initiate dialysis due to inadequate blood flow even after the intervention (the criteria could be lower for children or patients with low body weight).

Thrombosis：

1) Intrinsic catheter thrombosis: a thrombus is formed and attached to the inner or outer surface of the catheter (including the thrombi in the lumen or at the tip of the catheter). 2) Extrinsic

catheter thrombosis: thrombus caused by the presence of a catheter in the atrium, mural or central vein.

Catheter malposition or kinking. Position of the catheter tip was at the wrong place or moved during indwelling, or the catheter curved or folded.

Fibrin shell. Fibrin shell is a membranoid substance made up of endothelial cells, smooth muscle cells and collagen wrapping around the central venous catheter, which can happen within 24 hours after catheter indwelling [12]. Fibrin shells could cause several complications including catheter dysfunction, infection, stenosis of central vein and pulmonary embolism after catheter removal. The presence of fibrin shells was evaluated by digital subtraction angiography (DSA).

Central vein stenosis

Damage caused by the dialysis catheter after indwelling, along with comorbidities that could induce stenosis of the central vein and thus cause obstruction syndrome, which in turn caused a series of symptoms and signs including swelling of the limbs, head and neck after stenosis of the vena cava system, and caused ulcer and infection in the limbs and encephaledema in severe cases. Clinical symptoms, Doppler ultrasound examinations and angiography were needed for diagnosis, and angiography could confirm the location and extent of the obstruction.

Statistical analysis

SPSS 17.0 (SPSS Inc., Chicago, IL, USA) was used for the data management and analysis. General characteristics of the patients are presented as means and standard divisions or frequencies and percentages. Incidence rates per 1000 catheter-days were calculated for catheter complications. Categorical variables were compared using a chi-square test. Logistic regression was used to investigate the risk factors influencing the outcomes of catheter-infection,

catheter-dysfunction, and central vein stenosis, which were the dependent variables; the independent variables were patient characteristics (including treatment) and parameters surrounding catheter placement. The detailed independent variables investigated were age (≤17, 18-44, 45~59,≥60), gender (female vs male), registered residency (urban vs rural), marital status (unmarried vs married), primary disease (non-diabetes vs diabetes), education degree (university, middle school, below primary school), occupation (farmer and unemployment vs others), source of payment for medical costs (self-paying, new rural cooperative medical system, medical insurance), serum albumin level (＞40 g/L, 35~40 g/L,＜35g/L), serum ferritin level (<100ng/ml, 100~800ng/ml, >800ng/ml), hemoglobin level (<60g/L, 60~90g/L, >90g/L), duration of hemodialysis (≥48 months, 24~48 months,＜24 months), hemodialysis frequency (3/week, 5/ 2 weeks, 2/week, 3/2 weeks, ≤1/week), Hemodialysis frequency, nephropathy visit before dialysis treatment (yes vs no), establishing long-term vascular access in advance informed by doctors (yes vs no), taking drugs preventing catheter thrombus orally (yes vs no), imaging examination after catheter implantation (yes vs no), type of hemodialysis catheter (NTHCs vs TVCs), catheter puncturing approach vessel (femoral vein, internal jugular vein, external jugular vein, subclavian vein), catheterized surgery location (left vs right side), catheterized surgery times (≥3,2,1). The results are presented as odds ratios (OR) and 95% confidence intervals (95%CI). Two-tailed P-values <0.05 were considered statistically significant.

Results

Characteristics of the patients

Table 1 presents the characteristics of 865 patients included in the present study between

October 2013 and October 2014, 564 being indwelled with NTHCs for 136.2±67.4 days and 385 with TVCs for 1052.3±371.3 days. Patients were aged 49.53±18.42 years. There were 495 (57.2%) males and 370 females (42.8%). Among all patients, 386 (44.6%) were receiving help from the New Rural Cooperative Medical System, 319 (36.9%) had medical insurances, and 160 (18.5%) were self-paying for their medical care. The three most common causes of ESRD were diabetic kidney disease (n=236, 27.3%), primary nephropathy (n=143, 16.5%) and hypertensive nephropathy (n=96, 11.1%). At the time of the study, patients had undergone dialysis for a median of 26.5 months (range: 15 days to 18 years). The hemodialysis frequency was twice per week in 375 (43.4%), 3 times per week in 182 (21.0%), three times per two weeks in 121 (14.0%) and five times per two weeks in 145 (18.6%) patients.

Complications

The overall incidence of catheter infection was 7.74/1000 catheter-days or 38.61% of all patients in the study. The overall incidence rate of catheter dysfunction was 10.58/1000 catheter-days or 56.65% of the patients. The overall incidence rate of central vein stenosis was 0.68/1000 catheter-days or 8.79% of the patients.

Univariate analysis of factors involved in catheter-related complications

Age (≤17, 18～44, 45~59, ≥60; OR=0.427, 95%CI: 0.242～0.631, *P*=0.041), primary disease (non-diabetes vs diabetes; OR=0.416, 95%CI: 0.262～0.826, *P*<0.01), education level (below primary school vs university; OR=2.405, 95%CI: 1.373～4.214, *P*=0.002), registered residence (urban vs rural; OR=0.250, 95%CI: 0.157～0.398, *P*<0.01), nephropathy visit before dialysis treatment (yes vs no; OR=0.110, 95%CI: 0.064～0.189, *P*<0.01), pre-established permanent (yes vs no; OR=0.242, 95%CI: 0.154～0.381, *P*<0.01)，taking drugs preventing

catheter thrombus orally (yes vs no; OR=0.218, 95%CI: 0.125～0.379, *P*<0.01)，albumin (＞40 g/L, 35~40 g/L,＜35g/L；OR=0.400, 95%CI: 0.300～0.534, *P*<0.01)，ferritin (<100ng/ml, 100~800ng/ml, >800ng/ml; OR=1.857, 95%CI: 1.375～2.508, *P*<0.01) were associated with catheter infection (Table 2).

Registered residence (urban vs rural; OR=0.218, 95%CI: 0.137～0.345, *P*<0.01), medical costs (new rural cooperative medical system vs medical insurance; OR=3.762, 95%CI: 0.517～6.319, *P*=0.047; self-paying vs medical insurance; OR=6.412, 95%CI: 3.309～12.076, *P*=0.017), nephropathy visit before dialysis treatment (yes vs no; OR=0.056, 95%CI: 0.033～0.097, *P*<0.01), pre-established permanent vascular access (yes vs no; OR=0.114, 95%CI: 0.063～0.208, *P*<0.01), catheter type (NTHCs vs TVCs; OR=1.793, 95%CI: 1.510～2.231, *P*=0.031), catheter position (right vs left; OR=0.067, 95%CI: 0.034～0.130, *P*<0.01), imaging examination after catheter implantation (no vs yes; OR=2.827, 95%CI: 1.804～4.430, *P*<0.01), catheter puncturing approach vessels (internal jugular venous vs femoral vein; OR=0.126, 95%CI: 0.044～0.361, *P*<0.01; external jugular vein vs femoral vein; OR=0.06, 95%CI: 0.017～0.216, *P*<0.01; subclavian vein vs femoral vein; OR=0.094, 95%CI: 0.027～0.332, *P*<0.01), taking drugs preventing catheter thrombus orally (yes vs no; OR=0.100, 95%CI: 0.059～0.168, *P*<0.01), hemoglobin (<60g/L, 60~90g/L, >90g/L; OR=1.421, 95%CI: 1.318～1.558, *P*<0.01) were associated with catheter dysfunction (Table 2).

Primary disease (non-diabetes vs diabetes; OR=0.692, 95%CI: 0.148～0.871, *P*<0.01), nephropathy visit before dialysis treatment (yes vs no; OR=0.249, 95%CI: 0.148～0.420, *P*<0.01), pre-established permanent vascular access (yes vs no; OR=0.225, 95%CI: 0.140～

0.362, P<0.01), catheter position (right vs left; OR=0.325, 95%CI: 0.204～0.516, P<0.01), number of indwelling (≥3, 2, 1; OR=2.471, 95%CI: 1.818～3.360, P<0.01), taking drugs preventing catheter thrombus orally (yes vs no; OR=0.189, 95%CI: 0.089～0.362, P<0.01) were associated with central vein stenosis (Table 2).

Multivariate analysis of factors involved in catheter-related complications

The results of multivariate analysis are presented in Table 3.

Analysis of the relationship between independent variables and catheter infection by the logistic regression model showed that there were independent relationships between catheter infection and patients age, OR was 0.351 (95%CI 0.136～0.674), older patients had a higher catheter infection risk; the patient's registered residency, OR was 0.250 (95%CI 0.120～0.520), the catheter infection risk for rural registered residents was higher than for urban registered residents; primary disease, OR was 0.379 (95%CI 0.176～0.818), the catheter infection risk for patients with primary diabetes was higher than for patients without primary diabetes; patients with higher education levels had a lower catheter infection risk, OR was 10.757 (95%CI 3.637～31.817) for primary school vs college; nephropathy visit before dialysis treatment and establishing a long-term vascular access in advance were protective factors for catheter infection, OR was 0.22 (95%CI 0.096～0.502) and 0.401 (95%CI 0.193～0.832) respectively; taking drugs preventing catheter thrombus orally was a protective factor for catheter infection, OR was 0.611 (95%CI 0.404～0.923); the catheter infection risk for patients not taking drugs preventing catheter thrombus orally was higher than the patients taking drugs preventing catheter thrombus orally; serum protein level, OR was 0.142 (95%CI 0.085～0.237), serum ferritin level, OR was 2.162 (95%CI 1.412～23.308), patients with lower serum protein levels and higher serum ferritin

levels had higher risks of catheter infection.

Analysis of the relationship between independent variables and catheter dysfunction by the logistic regression model showed that there were independent relationships between catheter dysfunction and the following factors: registered residency, OR was 0.021 (95%CI 0.004～0.101), and the risk of catheter dysfunction for rural patients was higher than urban patients; taking drugs preventing catheter thrombus orally, OR was 0.106 (95%CI 0.041～0.274), the risk of catheter dysfunction for patients not taking drugs was obviously higher than the one for patients taking drugs; imaging examination after catheter implantation, OR was 2.631 (95%CI 1.293～5.354), the risk for patients without imaging examination after catheter implantation was significantly higher; for catheter type, NTHCs had higher risk than TVCs (OR=3.493, 95%CI: 1.358-8.983); patients had medical insurance had lower risk than patients who were self-paying (OR=13.416, 95%CI: 2.541 ～ 70.827); nephropathy visit before dialysis treatment and establishing a long-term vascular access in advance were protective factors for catheter dysfunction, OR was 0.048 (95%CI 0.018 ～ 0.124) and 0.025 (95%CI 0.006 ～ 0.109) respectively; left- or right-side catheterization, OR was 0.024 (95%CI 0.007～0.080) and the risk for catheterization on the right was lower; for catheter puncturing approach vessels, the femoral vein had a higher catheter dysfunction risk than other vessels (internal jugular venous vs femoral vein, OR=0.029, 95%CI: 0.005～0.179; external jugular vein vs femoral vein, OR=0.011, 95%CI: 0.001～0.089; subclavian vein vs femoral vein, OR=0.015, 95%CI: 0.002～0.125); hemoglobin level, OR was 2.276 (95%CI 1.101～4.794), and patients with higher levels were easier to tolerate it.

Analysis of the relationship between independent variables and central vein stenosis by the logistic regression model showed that there were independent relationships between central vein

stenosis and the following factors: catheterization frequency, OR was 1.827 (95%CI 1.175～2.841), the risk for patients with multiple punctures was higher; orally taking drugs preventing catheter thrombus, OR was 0.416 (95%CI 1.261～0.875), and the risk for patients not taking drugs was higher than that for patients taking drugs; nephropathy visit before dialysis treatment and establishing a long-term vascular access in advance were protective factors for central vein stenosis, OR were 0.319 (95%CI 0.119～0.855) and 0.162 (95%CI 0.084～0.312) respectively; left- or right-side catheterization, the OR was 0.514 (95%CI 0.268～0.986), the risk on the left was higher than the one on the right; primary disease, OR was 0.427 (95%CI 0.175～0.841), the risk for patients with diabetes mellitus was obviously higher than non-diabetic patients.

Complications according to the type of catheter: TVCs or NTHCs

There were 865 patients included in this study, in whom NTHCs were implanted 564 times, and TVCs 385 times; the monitoring times were 43051 catheter days (NTHCs) and 90758 catheter days (TVCs). Serious acute complications in the 949 total cases were rare. Only 2 patients experienced hemopneumothorax as a consequence of internal jugular vein cannulation and 1 patient experienced a hematoma due to femoral vein cannulation. All patients were fully recovered from these complications without removal of the hemodialysis catheter.

The incidence of infection related to TVCs was 5.39/1000 catheter days, and 30.29% of patients, which was lower than that of NTHCs which was 12.71/1000 catheter days, and 44.92% of patients (both $P<0.01$); incidence of catheter exit-site infection related to NTHCs was 9.15/1000 catheter days, and 39.63% of patients, higher than the rate of TVCs, which was 5.06/1000 catheter days, and 15.55% of patients (both $P<0.01$); because NTHCs does not generate any subcutaneous tunnels thus it is hard to compare with TVCs on the incidence of

subcutaneous tunnel infection, which was 2.73/1000 catheter days, and 12.87% of patients; incidence of catheter related bloodstream infections related to TVCs was 6.51/1000 catheter days, and 34.85% of patients, higher than the rate of NTHCs, which was 3.95/1000 catheter days, and was 17.48% of patients (both $P<0.01$). The incidence of NTHCs dysfunction was 14.68/1000 catheter days, and the incidence in patients was 65.65%, higher than those of TVCs dysfunction, which was 8.64/1000 catheter days, and 44.77% of patients (both $P<0.01$); incidence of NTHCs thrombus was 14.87/1000 catheter days, the incidence of patients was 57.72%, the incidence of NTHCs kinking or malposition was 4.41/1000 catheter days, 25.41% of patients, higher than those of TVCs which was 7.87/1000 catheter days, 38.87% of patients and 2.13/1000 catheter days, 11.0% of patients (both $P<0.01$); the incidence of TVCs fibrin shells was 2.21/1000 catheter days, 38.1% of patients, higher than that of NTHC fibrin shells, which was 1.67/1000 catheter days, 13.62% of patients ($P=0.040$ for catheter days; $P<0.01$ for patients). The incidence of TVCs central venous stenosis was 0.79/1000 catheter days, the incidence of patients was 15.28%, higher than the incidence of NTHCs, which was 0.44/1000 catheter days, 3.86% of patients ($P=0.021$ for catheter days; $P<0.01$ for patients).

Complications based on the catheter insertion site

Table 4 shows the incidence of complications with TVCs based on the catheter insertion site: In terms of catheter infection, there were no significant differences in the incidence of catheters inserted at the right internal jugular vein, left internal jugular vein, external jugular vein, and subclavian vein ($P=0.196$ for catheter days; $P=0.992$ for patients). The incidence of thrombosis ($P<0.01$ for catheter days; $P=0.017$ for patients), and the incidence of malpositioned or kinked catheters ($P=0.024$ for catheter days; $P=0.001$ for patients) were higher in the left internal jugular vein than the right internal jugular vein, external jugular vein, and subclavian vein; the

incidences of fibrin shells (P=0.993 for catheter days; P=0.999 for patients) were not significantly different between puncture approaches; the incidence of right internal jugular vein central venous stenosis was (P=0.036 for catheter days; P=0.004 for patients) lower than in the left internal jugular vein, external jugular vein, and subclavian vein; the incidence of femoral vein catheter infection ($P<0.01$ for catheter days; P=0.042 for patients), the incidence of thrombus ($P<0.01$ for catheter days; P=0.016 for patients) and the incidence of malpositioned or kinked catheters (P=0.036 for catheter days) were much higher than with other puncture approaches, inferior vena cava stenosis caused by femoral venipuncture was not seen.

Table 5 shows the incidence of complications with NTHCs based on catheter insertion site. For catheter infection the right internal jugular vein, left internal jugular vein, and subclavian vein (P=0.972 for catheter days; P=0.998 for patients), venous thrombosis (P=0.991 for catheter days; P=0.988 for patients) showed no significant differences; and the incidence of femoral vein (both P=0.01), and the incidence of thrombus (both P=0.01) were much higher than that of the internal jugular vein, and subclavian vein, but not lower than the incidence of fibrin shell in the femoral vein (both P=0.01); the incidence of malpositioned or kinked catheter was highest in the femoral vein ($P<0.01$ for catheter days; P=0.01 for patients), the incidence of malpositioned or kinked catheters in the left internal jugular vein was higher than those in the right internal jugular vein and subclavian vein ($P<0.01$ for catheter days; P=0.080 for patients); the incidences of (left and right side) internal jugular vein and central venous stenosis were not significantly different (P=0.310 for catheter days; P=0.343 for patients). Femoral vein NTHCs with inferior vena cava stenosis was not seen.

Complications related to the type of catheter

The incidence of catheter type-related complications are presented in Table 6. The incidences of infection (P=0.976 for catheter days; P=0.985 for patients) and fibrin shell formation (P=0.963 for catheter days; P=1.000 for patients) related to 4 types of TVCs were not significantly different; the highest incidence of catheter thrombosis was with the use of HemoSplit and the lowest incidence was with the use of Palindrome catheters ($P<0.01$ for catheter days;, P=0.002 for patients); the incidences of kinking or malposition using Permcath and Palindrome catheters were not significantly different (P=0.857 for catheter days; P=0.992 for patients), but higher than that of Cannon® Ⅱ Plus and HemoSplit catheters ($P<0.01$ for catheter days; P=0.030 for patients); incidence of central venous stenosis with Cannon® Ⅱ Plus catheter was lower than with other catheters (P=0.025 for catheter days; P=0.028 for patients); Kt/V values were higher in patients using Palindrome than any of the other 3 types of TVCs, however the difference was not statistically significant (P=0.990).

Among the 4 types of NTHCs, the incidence of catheter infection (P=0.971 for catheter days; P=1.000 for patients) and incidence of central venous stenosis (P=0.963 for catheter days; P=0.961 for patients) were not significantly different; the incidences of thrombus (P=0.988 for catheter days; P=1.000 for patients), catheters kinking or malposition (P=0.991 for catheter days; P=0.999 for patients) and fibrin shell formation (P=0.997 for catheter days; P=0.999 for patients) were also not significantly different between the 4 types of NTHCs; Kt/V values were not significantly different between the 4 types of NTHCs (P=0.965).

Discussion

The objective of the present study was to investigate the incidence and risk factors of

catheter-related complications in different districts and populations of Henan Province in China. The overall incidence was 7.74/1000 catheter-day or 38.61% of patients for catheter infections, 10.58/1000 catheter-day or 56.65% of patients for catheter dysfunction, and 0.68/1000 catheter-day or 8.79% of patients for central vein stenosis. Multivariate analysis showed that age, primary disease, education level, registered residence, nephropathy visit before dialysis and pre-established permanent vascular access, oral drugs for preventing thrombus, serum protein levels, and ferritin levels were independently associated with the risk of catheter infection. The registered place of residence, oral drugs for preventing thrombus, pre-established permanent vascular access, nephropathy visit before dialysis treatment, catheter position, imaging examination after catheter indwelling, catheter type, medical cost, catheter puncturing approach vessels and hemoglobin levels were independently associated with catheter dysfunction. Primary disease, pre-established permanent vascular access, oral drugs for preventing thrombus, number of indwelling surgeries, catheter position, and nephropathy visit before dialysis treatment were independently associated with central vein stenosis.

Previous studies showed that the rate of CRI was about 3.8-6.5 per 1000 catheter-days [13, 14]. However, the rate of CRI was higher in the present study. There are a few reasons that may be responsible for this higher rate. The first are the characteristics of the patients. The patients in this study were relatively older (mean age: 49.53±18.42 years) hence were generally associated with age-related multiple organ function damage, malnutrition, impaired immunity and feebleness, all of which could increase the risk of catheter infection. Diabetes is the most frequent primary disease (27.3%), and long-term diabetes is associated with peripheral vascular disorders, preventing AVF surgery and requiring the use of catheters for dialysis. The risk of CRI was increased by 60% in patients with diabetes [15]. Patients with higher education or

communication ability may be more concerned about the severity of their diseases and understand better about self-care of dialysis catheters. Urban living patients generally are highly educated than rural living ones. However, most of the patients included in the present study were from rural areas (57.5%), or with an education level of middle school or lower. Dialysis brings a heavy financial burden on patients. In the present study, most of the patients had medical insurance from the New Rural Cooperative Medical System (44.6%) or even had no medical insurance (18.5%).

The overall infection rate in the NTHCs group was significantly higher than in the TVCs group, which is supported by previous findings [14]. Indeed, longer indwelling time might have been the main reason causing a higher rate of CRBI in the TVCs group (1052.28±371.26 days) as compared with the NTHCs group (136.2±67.4 days). Oliver et al. [14] showed that the duration of catheter indwelling was a high risk factor of CRI. Weijmer et al. [16] suggested that for patients needing NTHCs for more than 2 weeks, the catheter should be changed to TVCs to reduce the risk of infection. Longer catheter indwelling time was generally associated with low educational level of the patients (they were not fully aware of the severity of the disease). In the present study, 85.5% of the patients experienced two or more surgeries for vascular access.

Catheter dysfunction is characterized by poor blood flow. Previous studies showed that 98% of catheter dysfunctions occurring within 2 weeks were caused by either a catheter embolism or a fibrin shell [4]. Suhocki et al. [17] reported that among 163 patients with catheter dysfunctions, 74.2% had catheter embolism and 23.3% had fibrin shell. Napalkov et al. [18] performed an investigation in 3213 patients using dialysis catheters and found that the incidence of thrombosis was 8.6/1000 catheter-day. In the present study, the overall incidence rate of catheter dysfunction was 10.58/1000 catheter-day for all patients, 8.64/1000 catheter-day for placed TVCs (which was

in accordance with previous studies) and 12.86/1000 catheter-day for placed NTHCs (which was substantially higher than previous studies). NTHC catheter type was a risk factor for catheter dysfunction in this study. Hyperlipidemia, arteriosclerosis, hematonosis and cancers can induce hypercoagulability [19]. In addition, patients with uremia generally have high homocysteine levels and microinflammation, which can increase thrombogenesis [19]. Too many indwelling surgeries could damage the vascular wall, and the exposure of endothelium could promote platelet adhesion and activate endogenous coagulation pathway, which could be further aggravated by the local disturbance of hemodynamics after catheter indwelling [20]. But we did not find the times of indwelling surgery to be associated with catheter dysfunction in this study. Fibrin shells may occur in all sorts of central venous catheters, which not only induce catheter dysfunction, but also induce a series of complications including infection, thrombogenesis, catheter removal and pulmonary embolism [21, 22]. Previous studies showed that the incidence of fibrin shells was generally high. In a study performed by Oliver et al. [23], 70% of the patients with indwelled catheters were with fibrin shell. Schon et al. [24] also showed that 38% of the patients with catheter dysfunction had a fibrin shell. In the present study, the incidence rate of fibrin shell was greatly lower than in previous studies, which was 3.69/1000 catheter or 2.18% of placed catheters for the patients in the NTHCs group and 3.81/1000 catheter-day or 2.41% of placed catheters for the ones in the TVCs group. Although treatment with drugs or fibrin dissection could restore partial catheter function in some cases, there are some disadvantages including the high recurrence rate after drug-therapy and the high cost of fibrin dissection. Therefore, although several clinicians speculated that catheter dysfunction could be associated with the formation of fibrin shell, the medical cost pushed the patients to replace dialysis catheter instead of performing further imaging examinations, which underestimated the diagnostic rate of fibrin shells.

The incidence of central vein stenosis can be as high as 25%-40% [25]. Several studies also showed that 95% of the patients with central vein stenosis had a history of catheter indwelling, while only 13.6% of the patients without history of catheter indwelling developed central vein stenosis, repeated indwelling surgeries could increase the incidence of central vein stenosis in dialysis patients by 3-fold [26]. After catheter indwelling, mechanical injuries to the vascular endothelium, secondary activation of platelet and coagulation pathways, changes in hemodynamics and extrinsic compression of catheter-surrounding tissues participated in the development of central vein stenosis [27]. Angiography is the gold standard for diagnosis of central vein stenosis [28]. In the present study, the overall incidence rate of central vein stenosis (0.68/1000 catheter-days) was relatively low, which could be due to a low diagnostic rate. Indeed, only patients with severe symptoms (including severe facial swelling, limb swelling, limb pain, and intracranial hypertension) were examined by angiography, while most patients without symptoms or only with mild symptoms were not diagnosed due to high medical costs or insufficient awareness from the clinicians. The incidence was significantly higher in patients using TVCs (0.79/1000 catheter-days) compared those with NTHCs (0.44/1000 catheter-days, $P<0.05$), which might be associated with the stimulations to the vascular wall caused by the long duration of TVCs indwelling. Diabetes is an important risk factor for central vein stenosis, which could be caused by long-term influences of high glucose, chronic inflammation, and lipid metabolism disorders, increasing the risk of angiosclerosis, vascular wall thickening, reduced elasticity, thrombogenesis and stenosis in diabetic patients on dialysis [29].

In this study, four different types of TVCs and four different types of NTHCs were used in the 14 participating hospitals. Since no specific coating was applied to each of the four types of TVCs to prevent infection and thrombosis, and since the indwelling duration of these four types

of TVCs was similar, no significant difference in the incidence rate of catheter infection was found among these four types of TVCs. However, the incidence of catheter embolism was significantly higher with the HemoSplit™ catheter compared with the other types, and the incidence of catheter embolism in patients using the Palindrome™ catheter was the lowest, which could be associated with different designs of the side holes at the tip of the catheters. The side holes in Palindrome™ catheter are relatively large rectangles made by laser notching, which are relatively difficult for thrombi to adhere to [30], while the side holes in the HemoSplit™ catheter are relatively small round holes that could be easily adhered by thrombi. The texture and cuff rings are identical in the Palindrome™ and Permcath™ catheters, of which the rates of catheter kinking and malposition were significantly higher compared with the other two types of TVCs. The specific "retrograde design" of the Cannon II Plus catheter [31] makes sure that the cuff ring is fixed to the clavicle, while the cuff ring in the HemoSplit™ catheter can be closely connected with the adjacent tissues. Therefore, these two catheters had a lower risk of kinking and malposition. The incidence rate of central vein stenosis with the Cannon II Plus™ catheter was the lowest among all the four types of TVCs, which could be associated with the tip of the catheter that was placed in the right atrium so that the stimulation to the superior vena cava was relatively small. There were no significant differences in the incidence of any complications between the four different NTHCs used in this study.

This present study has several limitations. First, there remains residual confounding from unmeasured variables such as medical therapy, nutritional status of the patients, biochemical indexes and psychosocial factors. Second, Henan Province covers a large area and has a large population, and the levels of economics, culture and healthcare vary greatly among different districts. Since all 14 participating hospitals included were from the districts with relatively high

economic level, the epidemiological features of catheter-related complications could be different from remote areas or other districts with relatively low economic level. Therefore, the incidence of catheter-related complications could be underestimated in the present study.

In conclusion, patients receiving dialysis in Henan Province had a high rate of dialysis catheter use with long duration of temporary catheter indwelling, which resulted in a high incidence of catheter-related complications. Therefore, the healthcare administration needs to develop policies for establishing vascular access as soon as possible.

Authors' contributions

KW and ZSL have made substantial contributions to conception and design; KW, PW, XHL, XQL and ZSL have made substantial contributions to acquisition of data, or analysis and interpretation of data; KW and ZSL has been involved in drafting the manuscript or revising it critically for important intellectual content; all authors have given final approval of the version to be published.

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Competing interests

The authors declare that they have no competing interests.

Data sharing statement

Technical appendix, statistical code and dataset are available from the corresponding author at the Dryad repository, which will provide a permanent, citable and open access repository for the dataset.

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Table 1. Patient characteristics

Characteristics	**Values** (N=865)
NTHCs	564
TVCs	385
Indwelling time (days)	
NTHCs	136.2±67.4
TVCs	1052.3±371.3
Permanent catheter	
Quinton Palindrome™	103 (24.4%)
Quinton Permcath™	91 (21.6%)
Arrow Cannon II Plus™	101 (29.1%)
Bard HemoSplit™	90 (24.9%)
Age (years)	49.53±18.42
≤18	126 (14.6%)
19-44	212 (24.5%)
45-59	236 (27.3%)
≥60	291 (33.6%)
Gender	
Male	495 (57.2%)
Female	370 (42.8%)
Marital status	
Married	487 (56.3%)
Single	285 (32.9%)
Widowed or divorced	93 (10.8%)
Education	
University	152 (17.6%)
Middle school	481 (55.6%)
Below primary school	232 (26.8%)
Occupation	
Farmer	352 (40.7%)
Worked	124 (14.3%)
Office worker	95 (11.0%)
Retired	165 (19.1%)
Unemployed	129 (14.9%)
Registered residence	
Rural	497 (57.5%)
Urban	368 (42.5%)
Medical costs	
New Rural Cooperative Medical System	386 (44.6%)
Medical insurance	319 (36.9%)
Self-paying	160 (18.5%)
Primary disease	
Diabetic kidney disease	236 (27.3%)
Primary nephropathy	143 (16.5%)
Hypertensive nephropathy	96 (11.1%)

Acute renal failure	44 (5.1%)
Obstructive nephropathy	72 (8.3%)
Renal tubular interstitial disease	62 (7.2%)
Drug-induced renal damage	39 (4.5%)
Myeloma	24 (2.8%)
Others	103 (11.9%)
Hemodialysis duration, median (range)	26.5 months (15 day-18 years)
Hemodialysis frequency	
Twice per week	375 (43.4%)
Three times per week	182 (21.0%)
Three times per two weeks	121 (14.0%)
Five times per two weeks	145 (16.8%)

Table 2. Univariate logistic regression of factors influencing the development of dialysis catheter-related complications

Variables	Catheter-infection			Catheter dysfunction			Central vein stenosis		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age	0.427	0.242-0.631	0.041	1.157	0.745-1.797	0.516	1.469	0.934-2.310	0.096
Gender	0.752	0.491-1.152	0.19	1.046	0.680-1.610	0.837	1.132	0.723-1.772	0.588
Primary disease	0.416	0.262-0.826	< 0.01	0.738	0.266-1.613	0.125	0.692	0.148-0.871	< 0.01
Marriage	1.109	0.701-1.754	0.658	1.318	0.819-2.122	0.256	1.377	0.854-2.221	0.189
Education									
University			< 0.01			0.225			0.150
Middle school	0.669	0.406-1.104	0.116	0.668	0.411-1.086	0.104	0.669	0.406-1.104	0.116
Below primary school	2.405	1.373-4.214	0.002	0.962	0.538-1.719	0.895	0.392	0.204-0.753	0.072
Occupation	1.380	0.892-2.136	0.148	1.151	0.743-1.783	0.528	1.333	0.838-2.121	0.224
Registered residence	0.250	0.157-0.398	< 0.01	0.218	0.137-0.345	< 0.01	0.352	0.217-0.571	0.092
Medical costs									
New Rural Cooperative Medical System			0.315			0.032			0.546
Medical insurance	1.475	1.273-2.138	0.076	3.762	0.517-6.319	0.047	1.545	0.612-1.941	0.239
Self-paying	1.958	0.512-2.731	0.089	6.412	3.309-12.076	0.017	1.368	0.203-1.628	0.202
Frequency of dialysis	0.882	0.735-1.059	0.180	0.905	0.750-1.092	0.296	0.937	0.772-1.136	0.507
Duration of hemodialysis	1.716	0.782-3.769	0.178	1.703	0.700-4.144	0.240	3.073	1.387-6.807	0.063
Nephropathy visit before dialysis treatment	0.110	0.064-0.189	< 0.01	0.056	0.033-0.097	< 0.01	0.249	0.148-0.420	< 0.01
Pre-established permanent vascular access	0.242	0.154-0.381	< 0.01	0.114	0.063-0.208	< 0.01	0.225	0.140-0.362	< 0.01
Catheter type	0.654	0.425-1.005	0.052	1.793	1.510-2.231	0.031	1.082	0.685-1.708	0.736
Catheter position	0.521	0.338-0.804	0.603	0.067	0.034-0.130	< 0.01	0.325	0.204-0.516	< 0.01
Number of indwelling surgeries	1.148	0.888-1.485	0.292	1.669	1.276-2.183	0.086	2.471	1.818-3.360	< 0.01
Imaging	2.720	1.696-4.363	0.728	2.827	1.804-4.430	<	2.106	0.148-0.420	0.083

examination after catheter implantation						0.01			
Catheter puncturing approach vessels									
Femoral vein			0.227			< 0.01			0.110
Internal jugular venous	0.835	0.460-1.516	0.554	0.126	0.044-0.361	< 0.01	0.37	0.202-0.678	0.172
External jugular vein	0.363	0.126-1.047	0.061	0.060	0.017-0.216	< 0.010	0.355	0.128-0.984	0.471
Subclavian vein	0.572	0.219-1.495	0.255	0.094	0.027-0.332	< 0.01	0.321	0.117-0.882	0.282
Taking drugs preventing catheter thrombus orally	0.218	0.125-0.379	< 0.01	0.100	0.059-0.168	< 0.01	0.189	0.089-0.362	< 0.01
Hemoglobin	0.400	0.300-0.534	0.061	1.421	1.318-1.558	< 0.01	0.514	0.383-0.689	0.078
Albumin	0.151	0.102-0.224	< 0.01	0.369	0.278-0.489	0.572	0.585	0.441-0.777	0.347
Ferritin	1.857	1.375-2.508	< 0.01	0.96	0.717-1.286	0.786	0.898	0.663-1.218	0.49

Table 3. Multivariate logistic regression of factors influencing the development of dialysis catheter-related complications

Independent variables	OR	95% CI	*P* Value
Catheter infection			
Age	0.351	0.136-0.674	0.006
Registered residency	0.25	0.12-0.52	<0.01
Primary disease	0.379	0.176-0.818	0.013
Education degree	0.334	0.198-0.565	<0.01
University			<0.01
Middle school	1.224	0.547-2.736	0.623
Below primary school	10.757	3.637-31.817	<0.01
Nephropathy visit before dialysis treatment	0.22	0.096-0.502	<0.01
Establishing long-term vascular access in advance	0.401	0.193-0.832	0.014
Taking drugs preventing catheter thrombus orally	0.611	0.404-0.923	0.019
Albumin	0.142	0.085-0.237	<0.01
Ferritin	2.162	1.412-3.308	<0.01
Catheter dysfunction			
Registered resident	0.21	0.045-1.013	<0.01
Taking drugs preventing catheter thrombus orally	0.106	0.041-0.274	<0.01
Imaging examination after catheter implantation	2.631	1.293-5.354	0.008
Catheter type	3.493	1.358-8.983	0.009
Medical costs			
Medical insurance			0.004
New Rural Cooperative Medical System	0.949	0.265-3.403	0.936
Self-paying	13.416	2.541-70.827	0.002
Nephropathy visit before dialysis treatment	0.048	0.018-0.124	<0.01
Establishing long-term vascular access in advance	0.025	0.006-0.109	<0.01
Catheter left or right	0.024	0.007-0.080	<0.01
Catheter puncturing approach vessels			
Femoral vein			<0.01
Internal jugular venous	0.029	0.005-0.179	<0.01
External jugular vein	0.011	0.001-0.089	<0.01
Subclavian vein	0.015	0.002-0.125	<0.01
Hemoglobin	2.276	1.101-4.749	0.012
Central vein stenosis			
Catheterized surgery times	1.827	1.175-2.841	0.007
Taking drugs preventing catheter thrombus orally	0.416	0.261-0.875	0.043
Nephropathy visit before dialysis treatment	0.319	0.119-0.855	0.023
Establishing long-term vascular access in advance	0.162	0.084-0.312	<0.01
Left- or right- catheterization	0.514	0.268-0.986	0.045
Primary disease	0.427	0.175-0.841	0.007

Table 4. Morbidity of complications related to TVCs

Catheter-related complications			TVCs				
			Right internal jugular venous	Left internal jugular venous	Femoral vein	External jugular vein	Subclavian vein
Infection	Exit-site infection	(%)	14.35	15.31	37.5	16	16.22
		times/1000 catheter day	4.93	5.06	10.68	5.26	5.16
	Tunnel infection	(%)	11.96	13.27	18.75	12	13.51
		times/1000 catheter day	2.76	2.68	3.56	2.72	2.75
	CRBI	(%)	34.45	34.70	43.75	36	35.14
		times/1000 catheter day	6.69	6.49	10.08	6.62	6.42
Dysfunction	Thrombus	(%)	39.71	58.16	62.5	40	37.84
		times/1000 catheter day	7.96	13.94	14.83	7.81	7.68
	Fibrin shell	(%)	38.76	37.76	37.5	36	37.84
		times/1000 catheter day	2.15	2.03	2.08	2.21	2.29
	Malposition or kinking	(%)	11.48	29.51	43.75	12	13.51
		times/1000 catheter day	2.07	3.25	3.26	2.21	2.19
Central venous stenosis		(%)	12.44	27.55	0	28	27.03
		times/1000 catheter day	0.59	1.17	0	1.19	1.15

Note: fibrin shell and Central venous stenosis need to be proofed via imaging examination before being taken into statistical analysis.

Table 5. Morbidity of NTHC related complications

Catheter-related complications			NTHCs			
			Right internal jugular venous	Left internal jugular venous	Femoral vein	Subclavian vein
Infection	Exit-site infection	(%)	36.7	36.2	48.37	35.48
		times/1000 catheter day	8.79	8.54	19.66	8.85
	Tunnel infection	(%)	/	/	/	/
		times/1000 catheter day	/	/	/	/
	CRBI	(%)	16.51	17.39	29.77	17.74
		times/1000 catheter day	3.57	3.61	9.93	3.75
Dysfunction	Thrombus	(%)	58.7	59.42	78.6	58.06
		times/1000 catheter day	14.74	15	29.98	14.79
	Fibrin shell	(%)	13.76	14.49	4.19	14.53
		times/1000 catheter day	1.53	1.9	0.39	1.69
	Malposition or kinking	(%)	24.31	37.68	45.12	24.19
		times/1000 catheter day	4.37	10.06	19.86S	4.86T
Central venous stenosis		(%)	3.67	4.35	0	8.06
		times/1000 catheter day	0.45	0.27	0	0.62

Table 6. Morbidity of types of catheter related complications

Catheter-related complications			TVC types			NTHC types				
			Palindrome™	Permcath™	Cannon® II Plus	HemoSplit™	ARROW	DIALL	ABEL	TYCO
Infection	Exit-site infection	(%)	15.69	15.38	15.24	16.09	36.08	36.2	35.97	35.58
		times/1000 catheter day	5.12	5.08	4.97	5.17	8.96	9.08	9.05	8.82
	Tunnel infection	(%)	12.75	13.19	12.38	13.79	/	/	/	/
		times/1000 catheter day	2.74	2.7	2.75	2.83	/	/	/	/
	CRBI	(%)	35.29	35.16	35.24	35.63	17.09	17.18	17.27	17.31
		times/1000 catheter day	6.53	6.43	6.5	6.68	3.48	3.54	4.05	3.65
Catheter dysfunction	Thrombus	(%)	22.55	38.46	39.05	49.42	57.59	57.67	57.55	57.69
		times/1000 catheter day	5.32	8.76	7.31	9.8	15.01	15.03	14.51	14.86
	Fibrin shell	(%)	38.24	38.46	38.1	37.93	13.92	14.11	13.67	13.46
		times/1000 catheter day	2.25	2.06	2.1	2.07	1.49	1.53	1.6	1.51
	Malposition or kinking	(%)	18.63	18.68	8.57	10.34	31.01	30.67	30.22	30.77
		times/1000 catheter day	2.73	2.66	1.47	1.51	8.54	8.52	8.29	8.19
Central venous stenosis		(%)	14.71	15.38	3.81	14.94	3.8	4.91	4.32	3.85
		times/1000 catheter day	0.75	0.84	0.24	0.88	0.5	0.64	0.57	0.5
Kt/V			1.40±0.73	1.39±0.19	1.38±0.13	1.38±0.17	1.06±0.07	1.05±0.07	1.06±0.13	1.06±0.08

STARD checklist for reporting of studies of diagnostic accuracy

(version January 2003)

Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	N/A
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	N/A
METHODS			
Participants	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	6-7
	4	Participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	6-7
	5	Participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in item 3 and 4? If not, specify how participants were further selected.	6-7
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	N/A
Test methods	7	The reference standard and its rationale.	N/A
	8	Technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	9-10
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	N/A
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	N/A
	11	Whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	N/A
Statistical methods	12	Methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	N/A
	13	Methods for calculating test reproducibility, if done.	N/A
RESULTS			
Participants	14	When study was performed, including beginning and end dates of recruitment.	12
	15	Clinical and demographic characteristics of the study population (at least information on age, gender, spectrum of presenting symptoms).	12
	16	The number of participants satisfying the criteria for inclusion who did or did not undergo the index tests and/or the reference standard; describe why participants failed to undergo either test (a flow diagram is strongly recommended).	N/A
Test results	17	Time-interval between the index tests and the reference standard, and any treatment administered in between.	N/A
	18	Distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	N/A
	19	A cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	N/A
	20	Any adverse events from performing the index tests or the reference standard.	N/A
Estimates	21	Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	N/A
	22	How indeterminate results, missing data and outliers of the index tests were handled.	N/A
	23	Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	N/A
	24	Estimates of test reproducibility, if done.	N/A
DISCUSSION	25	Discuss the clinical applicability of the study findings.	15-21

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Epidemiology of hemodialysis catheter complications: survey of 865 uremic patients from 14 hemodialysis centers in Henan province of China

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Epidemiology of hemodialysis catheter complications: survey of 865 uremic patients from 14 hemodialysis centers in Henan province of China

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Running title: Hemodialysis catheter complications in China

Abstract

Objectives: To investigate the incidence rates and risk factors of catheter-related complications in different districts and populations of Henan Province (China).

Design: Cross-sectional.

Setting: Fourteen hospitals of Henan Province between October 2013 and October 2014.

Participants: 865 patients with renal dysfunctions using catheters for dialysis.

Main outcome measures: Main outcome measures were complications, risk factors and features of the patients. Catheter-related complications included: catheter-related infection (catheter exit site infection, catheter tunnel infection, and catheter-related bloodstream infection), catheter dysfunction (thrombosis, catheter malposition or kinking, and fibrin shell formation), and central vein stenosis.

Results: The overall incidence rate was 7.74/1000 catheter-day or 38.61% of all patients for catheter infections, 10.58/1000 catheter-day or 56.65% of all patients for catheter dysfunction, and 0.68/1000 catheter-day or 8.79% of all patients for central vein stenosis. Multivariate analysis showed that increased age, diabetes, education below primary level, rural registered residence, lack of a nephropathy visit before dialysis and pre-established permanent vascular access, not taking oral drugs for preventing catheter thrombus, lower serum albumin levels, and higher ferritin levels were independently associated with catheter infections. Rural registered residence, not taking oral drugs for preventing thrombus, lack of an imaging examination after catheter indwelling, non-tunnel hemodialysis catheters (NTHC) catheter type, lack of medical insurance, lack of nephropathy visit before dialysis and pre-established permanent vascular access, left-side catheter position, femoral vein approach vessel and lower hemoglobin level

were independently associated with catheter dysfunction. Diabetes, lack of nephropathy visit before dialysis and pre-established permanent vascular access, lack of oral drugs for preventing catheter thrombus, left-side catheter location and higher number of indwelling surgeries, were independently associated with central vein stenosis.

Conclusion: The rate of catheter-related complications was high in patients with end-stage renal disease (ESRD) in Henan Province. Based on identified factors, strategies should be implemented to decrease complication rates.

Keywords: end-stage renal disease; hemodialysis; catheter; complication.

Article summary

Strengths and limitations of this study

- This is a large study in different settings within the same geographical region.

- Comprehensive assessment of risk factors.

- Some residual confounders were not assessed (medical therapy, nutritional status, psychosocial factors).

- The incidence of catheter-related complications could be underestimated.

Introduction

Dialysis for end-stage kidney disease (ESRD) may be achieved using an arteriovenous fistula (AVF) or catheters [1]. However, the use of catheter is associated with increased all-cause mortality, mainly due to catheter-related infections (CRI) [2, 3]. According to guidelines, the proportion of patients with ESRD on dialysis who are using an AVF as permanent vascular access should be higher than 65% and the percentage of patients using dialysis catheter as permanent vascular access should be lower than 10% [1, 4]. However, using dialysis catheter is still very common. Indeed, according to the annual statistics of the United States Renal Data System (USRDS) [5], catheter was used in 62.6% of dialysis patients as vascular access for their first dialysis treatment in the USA, while only 16% of the patients were using AVF as vascular access for their first dialysis, and 81% of the patients were using dialysis catheter as the only vascular access or while waiting for the maturation of an AVF.

In addition to CRI, complications from catheter placement, catheter replacement and/or thrombolytic therapy, clots and emboli, exit site and tunnel irritation/infection, bacteremia and sepsis may all occur during catheter indwelling and after catheter removal, increasing mortality risk [6]. Indeed, CRI will happen in 2.5-5.5 patients per 1000 patient-days or 0.9-2.0 episodes per patient per year [7]. Catheter clotting and thrombosis will require plasminogen activator instillations in 3.0 cases per 1000 patient-days and catheter replacement in 1.1 cases per 1000 patient-days [8]. Thrombi may encroach into the right atrium and superior vena cava, causing pulmonary embolism and superior vena cava syndrome [9]. These complications not only threaten patients' safety and treatments' efficacy, but also waste medical resources. Catheter low flow may result in recirculation and under-dialysis; catheter placement may result in inflammation and immune reaction; catheter use may result in anemia, requiring erythropoietin; and frequent

dysfunction requires more care [6]. In 2007 alone, Medicare spending on ESRD neared $24 billion [10], with an estimated $1.8 billion spent annually on vascular access care [11].

Currently, there is no well-established register of dialysis catheters in China that reveals epidemiological data about catheter-related complications, risk factors and features of the patients. Therefore, the aim of the present cross-sectional study was to investigate the incidence rates and risk factors of catheter-related complications in different districts and populations of Henan Province (China) to help develop effective interventions and rational public health policies for the most efficient management of patients with ESRD undergoing dialysis using catheters.

Subjects and methods

Subjects

In the present cross-sectional study, 865 patients using catheters for dialysis in 14 hospitals of Henan Province between October 2013 and October 2014 were prospectively included. The 14 hemodialysis centers were: the First Affiliated Hospital of Zhengzhou University (n=125), the Third People's Hospital of Zhengzhou City (n=79), the Traditional Chinese Medicine Hospital of Henan Province (n=65), the Traditional Chinese Medicine Hospital of Zhengzhou city (n=36), the First Affiliated Hospital of Henan University of Science and Technology (n=66), Luoyang Eastern Hospital (n=56), Luoyang Center Hospital (n=42), Huaihe Hospital of Henan University (n=71), the First People's Hospital of Kaifeng City (n=52), the Second People's Hospital of Kaifeng City (n=47), the Puyang Oil Field General Hospital (n=49), the First People's Hospital of Xinxiang City (n=84), the Luohe Center Hospital (n=42), and the Sanmenxia Center Hospital

(n=51).

The inclusion criteria for the hospitals were: 1) at least 10 hemodialysis machines in the hemodialysis center; 2) at least 50 patients undergoing hemodialysis; and 3) at least 20 patients eligible for the study. The inclusion criteria for the patients were: 1) renal dysfunction caused by all sorts of reasons and undergoing hemodialysis using catheters for vascular access; 2) willingness to participate in the study, and with full capability of comprehension and communication; and 3) with complete records of previous vascular access for hemodialysis. Exclusion criteria were: 1) could not cooperate to the investigation; 2) previous medical records were not available; 3) <18 years of age or 4) with severe mental disorders or neurological diseases.

The study was approved by the ethics committee of the First Affiliated Hospital, Zhengzhou University. Written informed consent was obtained from each participant. Patient records/information was anonymized and de-identified prior to analysis.

Data collection

Data collected in the present study included: 1) general characteristics of the patients (age, gender, marriage, education, occupation, registered residence, provider payments, underlying disease, frequency of hemodialysis, duration of hemodialysis, and outcomes); 2) monitoring of the catheter (preparations of the vascular access before hemodialysis, reason for the first hemodialysis and the vascular access used, survival rates of non-tunnel hemodialysis catheters [NTHCs] and tunneled vascular catheters [TVCs], monitoring complications, and complications in different types of catheter); and 3) changes in vascular accesses (frequencies of vascular access changes and related reasons, records of catheters used in previous hemodialysis, duration of vascular access, and outcomes). The medical staff in the 14 participating hospitals was trained

in catheter monitoring and recording of epidemiological data. Standardized questionnaires were used to record patient's information and relevant data by the investigators in each hospital. Data were managed centrally at the Henan Blood Dialysis Quality Control Center. Any discrepancy was immediately solved upon data reception. Data was registered by trained registrars.

Indwelling of dialysis catheter

Aseptic practices were performed in the operating room by experienced physicians (the attending specialist in kidney diseases with a minimum of 1 year experience and 100 cases of catheter placement) from the Nephrology Department. The venipuncture site was prepared by disinfection with alcohol lipid-removal for 3 times, then by betadine (a common disinfector used in all 14 hospitals). There was no prophylactic use of antibiotics. The first choice for catheter placement was the right internal jugular vein, while other choices included the right external jugular vein, left internal/external jugular vein, subclavian vein, and femoral vein (according to the priority). Central vein catheterization was performed using the Seldinger technique (subcutaneous tunnel was needed for TVCs). With regard to NTHCs, single needle double-lumen catheters (ARROW: Arrow International Inc., Asheboro, NC, USA; DIALL: DIALL Medical Technology Co., Ltd. Zhengzhou, CHINA; ABLE: Guangdong Baihe Medical Technology Co., Ltd. Foshan，CHINA; TYCO：Covidien Co., Ltd. USA) were used, and the permanent indwelling catheters were placed with Quinton Palindrome™ (Covidien Co., Ltd. USA), Quinton Permcath™ (Covidien Co., Ltd. USA), Arrow Cannon II Plus™ (Arrow International Inc., Asheboro, NC, USA), and Bard HemoSplit™ (C. R. Bard, Inc.USA). The length and size of catheters were decided according to age, height and site of catheter indwelling. The type of catheter was decided by the hospital. Local infiltration anesthesia was chosen as the primary anesthesia method, while general anesthesia could also be used for children or uncooperative

patients. Evaluation of the patient was performed before indwelling. Doppler ultrasonography-guided puncture or venography-assisted catheter indwelling was used in patients with vascular malformation, stenosis, and occlusion of the central vein or using pacemaker.

Hemodialysis and catheter care

Patients were dialyzed 2-4 times per week, 4-5 hours per treatment. Blood flow was 5 ml/kg per min, and the dialysate flow was 300-500 ml/min. Hollow-fiber dialyzers were selected according to the patients' body size (Fresenius®, Gambro® or Nipro® hemodialysis machines). A standard bicarbonate buffer was used as dialysate buffer. Microbiological water purity was checked monthly to ensure compliance with tight chemical and microbiological standards (<0.1 cfu/ml and <0.03 EU/ml). Hemodialysis catheters were handled only during dialysis sessions with no irrigation between treatments. According to standard nursing procedures, the catheters' exit site and two ports care were cleaned with povidone iodine solution, applied with a Biopatch® (chlorhexidine-impregnated dressing), and covered with a permeable dressing at the end of each dialysis session. Each port of the catheter was filled with 5,000 U/ml of heparin solution according to the manufacturer's recommendation. Each time before opening the catheter, the exit site of the catheter was carefully checked for any redness, swelling, bleeding or exudate, and the patients were asked to report any episode of fever. In addition, the temperature of each patient was measured twice during dialysis. This process was repeated strictly for each hemodialysis treatment.

Definitions of dialysis catheter-related complications [12]

Dialysis catheter-related infection

Catheter exit site infection. Diagnosed: presence of pus, redness, induration, or tenderness within 2 cm around the catheter exit site, pus secretion culture was positive. Suspicious: presence of pus, redness, induration, or tenderness at the catheter exit site, yet pus secretion culture was negative. No signs of infection in gauze or sutures.

Catheter tunnel infection. Diagnosed: presence of pus, redness, tenderness, and/or induration (>2 cm) along the catheter tunnel, with a positive bacteria culture from secretions. Suspicious: presence of pus, redness, induration, and tenderness along the catheter tunnel, without a positive culture from secretions or infections in other loci.

Catheter-related bacteremia infection (CRBI). Diagnosed: the same microorganism grown from peripheral blood culture and catheter tip culture for at least once; or the count of colonies cultured from catheter lock solution is ⩾3-fold than the count from peripheral blood culture. Suspicious: positive blood cultures obtained from catheter lock solution and/or peripheral blood in a symptomatic patient, while no clinical evidence of infections in other loci.

Catheter dysfunction

Catheter dysfunction was diagnosed when at least one of the following criteria was met: 1) peak blood flow <200 ml/min for at least 30 min; 2) mean blood flow <250 ml/min during two consecutive dialysis; or 3) unable to initiate dialysis due to inadequate blood flow even after the intervention (the criteria could be lower for children or patients with low body weight).

Thrombosis：

1) Intrinsic catheter thrombosis: a thrombus is formed and attached to the inner or outer surface of the catheter (including the thrombi in the lumen or at the tip of the catheter). 2) Extrinsic

catheter thrombosis: thrombus caused by the presence of a catheter in the atrium, mural or central vein.

Catheter malposition or kinking. Position of the catheter tip was at the wrong place or moved during indwelling, or the catheter curved or folded.

Fibrin shell. Fibrin shell is a membranoid substance made up of endothelial cells, smooth muscle cells and collagen wrapping around the central venous catheter, which can happen within 24 hours after catheter indwelling [12]. Fibrin shells could cause several complications including catheter dysfunction, infection, stenosis of central vein and pulmonary embolism after catheter removal. The presence of fibrin shells was evaluated by digital subtraction angiography (DSA).

Central vein stenosis

Damage caused by the dialysis catheter after indwelling, along with comorbidities that could induce stenosis of the central vein and thus cause obstruction syndrome, which in turn caused a series of symptoms and signs including swelling of the limbs, head and neck after stenosis of the vena cava system, and caused ulcer and infection in the limbs and encephaledema in severe cases. Clinical symptoms, Doppler ultrasound examinations and angiography were needed for diagnosis, and angiography could confirm the location and extent of the obstruction.

Statistical analysis

SPSS 17.0 (SPSS Inc., Chicago, IL, USA) was used for the data management and analysis. General characteristics of the patients are presented as means and standard divisions or frequencies and percentages. Incidence rates per 1000 catheter-days were calculated for catheter complications. Categorical variables were compared using a chi-square test. Logistic regression was used to investigate the risk factors influencing the outcomes of catheter-infection,

catheter-dysfunction, and central vein stenosis, which were the dependent variables; the independent variables were patient characteristics (including treatment) and parameters surrounding catheter placement. The detailed independent variables investigated were age (≤17, 18-44, 45~59,≥60), gender (female vs male), registered residency (urban vs rural), marital status (unmarried vs married), primary disease (non-diabetes vs diabetes), education degree (university, middle school, below primary school), occupation (farmer and unemployment vs others), source of payment for medical costs (self-paying, new rural cooperative medical system, medical insurance), serum albumin level (＞40 g/L, 35~40 g/L,＜35g/L), serum ferritin level (<100ng/ml, 100~800ng/ml, >800ng/ml), hemoglobin level (<60g/L, 60~90g/L, >90g/L), duration of hemodialysis (≥48 months, 24~48 months,＜24 months), hemodialysis frequency (3/week, 5/ 2 weeks, 2/week, 3/2 weeks, ≤1/week), Hemodialysis frequency, nephropathy visit before dialysis treatment (yes vs no), establishing long-term vascular access in advance informed by doctors (yes vs no), taking drugs preventing catheter thrombus orally such as aspirin, clopidogrel or warfarin (yes vs no), imaging examination after catheter implantation (yes vs no), type of hemodialysis catheter (NTHCs vs TVCs), catheter puncturing approach vessel (femoral vein, internal jugular vein, external jugular vein, subclavian vein), catheterized surgery location (left vs right side), catheterized surgery times (≥3,2,1). The results are presented as odds ratios (OR) and 95% confidence intervals (95%CI). Two-tailed P-values <0.05 were considered statistically significant.

Results

Characteristics of the patients

Table 1 presents the characteristics of 865 patients included in the present study between October 2013 and October 2014, 564 being indwelled with NTHCs for 136.2±67.4 days and 385 with TVCs for 1052.3±371.3 days. Patients were aged 49.53±18.42 years. There were 495 (57.2%) males and 370 females (42.8%). Among all patients, 386 (44.6%) were receiving help from the New Rural Cooperative Medical System, 319 (36.9%) had medical insurances, and 160 (18.5%) were self-paying for their medical care. The three most common causes of ESRD were diabetic kidney disease (n=236, 27.3%), primary nephropathy (n=143, 16.5%) and hypertensive nephropathy (n=96, 11.1%). At the time of the study, patients had undergone dialysis for a median of 26.5 months (range: 15 days to 18 years). The hemodialysis frequency was twice per week in 375 (43.4%), 3 times per week in 182 (21.0%), three times per two weeks in 121 (14.0%) and five times per two weeks in 145 (18.6%) patients.

Complications

The overall incidence of catheter infection was 7.74/1000 catheter-days or 38.61% of all patients in the study. The overall incidence rate of catheter dysfunction was 10.58/1000 catheter-days or 56.65% of the patients. The overall incidence rate of central vein stenosis was 0.68/1000 catheter-days or 8.79% of the patients.

Univariate analysis of factors involved in catheter-related complications

Increased age (≤17, 18～44, 45~59, ≥60; OR=0.427, 95%CI: 0.242～0.631, *P*=0.041), diabetes (non-diabetes vs diabetes; OR=0.416, 95%CI: 0.262～0.826, *P*<0.01), below primary school education level (below primary school vs university; OR=2.405, 95%CI: 1.373～4.214, *P*=0.002), rural registered residence (urban vs rural; OR=0.250, 95%CI: 0.157～0.398, *P*<0.01), lack of a nephropathy visit before dialysis treatment (yes vs no; OR=0.110, 95%CI: 0.064～

0.189, *P*<0.01), lack of pre-established permanent vascular access (yes vs no; OR=0.242, 95%CI: 0.154～0.381, *P*<0.01)，not taking oral drugs to prevent catheter thrombus (yes vs no; OR=0.218, 95%CI: 0.125～0.379, *P*<0.01), low serumalbumin level (＞40 g/L, 35~40 g/L,＜35g/L；OR=0.400, 95%CI: 0.300～0.534, *P*<0.01) and high serum ferritin level (<100ng/ml, 100~800ng/ml, >800ng/ml; OR=1.857, 95%CI: 1.375～2.508, *P*<0.01) were associated with catheter infection (Table 2).

A rural registered residence (urban vs rural; OR=0.218, 95%CI: 0.137～0.345, *P*<0.01), lack of medical insurance (new rural cooperative medical system vs medical insurance; OR=3.762, 95%CI: 0.517～6.319, *P*=0.047; self-paying vs medical insurance; OR=6.412, 95%CI: 3.309～12.076, *P*=0.017), lack of a nephropathy visit before dialysis treatment (yes vs no; OR=0.056, 95%CI: 0.033～0.097, *P*<0.01), lack of pre-established permanent vascular access (yes vs no; OR=0.114, 95%CI: 0.063～0.208, *P*<0.01), NTHC catheter type (NTHCs vs TVCs; OR=1.793, 95%CI: 1.510～2.231, *P*=0.031), left-side catheter position (right vs left; OR=0.067, 95%CI: 0.034～0.130, *P*<0.01), lack of imaging examination after catheter implantation (no vs yes; OR=2.827, 95%CI: 1.804～4.430, *P*<0.01), femoral vein catheter puncturing approach vessel (internal jugular venous vs femoral vein; OR=0.126, 95%CI: 0.044～0.361, *P*<0.01; external jugular vein vs femoral vein; OR=0.06, 95%CI: 0.017～0.216, *P*<0.01; subclavian vein vs femoral vein; OR=0.094, 95%CI: 0.027～0.332, *P*<0.01), not taking oral drugs to prevent catheter thrombus (yes vs no; OR=0.100, 95%CI: 0.059～0.168, *P*<0.01) and lower hemoglobin level (<60g/L, 60~90g/L, >90g/L; OR=1.421, 95%CI: 1.318～1.558, *P*<0.01) were associated with catheter dysfunction (Table 2).

Diabetes (non-diabetes vs diabetes; OR=0.692, 95%CI: 0.148～0.871, *P*<0.01), lack of a nephropathy visit before dialysis treatment (yes vs no; OR=0.249, 95%CI: 0.148～0.420, *P*<0.01), lack of pre-established permanent vascular access (yes vs no; OR=0.225, 95%CI: 0.140～0.362, *P*<0.01), left-side catheter position (right vs left; OR=0.325, 95%CI: 0.204～0.516, *P*<0.01), increased number of indwelling (≥3, 2, 1; OR=2.471, 95%CI: 1.818～3.360, *P*<0.01) and not taking oral drugs to prevent catheter thrombus (yes vs no; OR=0.189, 95%CI: 0.089～0.362, *P*<0.01) were associated with central vein stenosis (Table 2).

Multivariate analysis of factors involved in catheter-related complications

The results of multivariate analysis are presented in Table 3.

Analysis of the relationship between independent variables and catheter infection by the logistic regression model showed that there were independent relationships between catheter infection and patients age, OR was 0.351 (95%CI 0.136～0.674), older patients had a higher catheter infection risk; the patient's registered residency, OR was 0.250 (95%CI 0.120～0.520), the catheter infection risk for rural registered residents was higher than for urban registered residents; primary disease, OR was 0.379 (95%CI 0.176～0.818), the catheter infection risk for patients with primary diabetes was higher than for patients without primary diabetes; patients with higher education levels had a lower catheter infection risk, OR was 10.757 (95%CI 3.637～31.817) for primary school vs college; nephropathy visit before dialysis treatment and establishing a long-term vascular access in advance were protective factors for catheter infection, OR was 0.22 (95%CI 0.096～0.502) and 0.401 (95%CI 0.193～0.832) respectively; taking drugs preventing catheter thrombus orally was a protective factor for catheter infection, OR was 0.611 (95%CI 0.404～0.923); the catheter infection risk for patients not taking drugs preventing

catheter thrombus orally was higher than the patients taking drugs preventing catheter thrombus orally; serum protein level, OR was 0.142 (95%CI 0.085～0.237), serum ferritin level, OR was 2.162 (95%CI 1.412～23.308), patients with lower serum protein levels and higher serum ferritin levels had higher risks of catheter infection.

Analysis of the relationship between independent variables and catheter dysfunction by the logistic regression model showed that there were independent relationships between catheter dysfunction and the following factors: registered residency, OR was 0.021 (95%CI 0.004～0.101), and the risk of catheter dysfunction for rural patients was higher than urban patients; taking drugs preventing catheter thrombus orally, OR was 0.106 (95%CI 0.041～0.274), the risk of catheter dysfunction for patients not taking drugs was obviously higher than the one for patients taking drugs; imaging examination after catheter implantation, OR was 2.631 (95%CI 1.293～5.354), the risk for patients without imaging examination after catheter implantation was significantly higher; for catheter type, NTHCs had higher risk than TVCs (OR=3.493, 95%CI: 1.358-8.983); patients had medical insurance had lower risk than patients who were self-paying (OR=13.416, 95%CI: 2.541 ～ 70.827); nephropathy visit before dialysis treatment and establishing a long-term vascular access in advance were protective factors for catheter dysfunction, OR was 0.048 (95%CI 0.018 ～ 0.124) and 0.025 (95%CI 0.006 ～ 0.109) respectively; left- or right-side catheterization, OR was 0.024 (95%CI 0.007～0.080) and the risk for catheterization on the right was lower; for catheter puncturing approach vessels, the femoral vein had a higher catheter dysfunction risk than other vessels (internal jugular venous vs femoral vein, OR=0.029, 95%CI: 0.005～0.179; external jugular vein vs femoral vein, OR=0.011, 95%CI: 0.001～0.089; subclavian vein vs femoral vein, OR=0.015, 95%CI: 0.002～0.125);

hemoglobin level, OR was 2.276 (95%CI 1.101～4.794), and patients with higher levels were easier to tolerate it.

Analysis of the relationship between independent variables and central vein stenosis by the logistic regression model showed that there were independent relationships between central vein stenosis and the following factors: catheterization frequency, OR was 1.827 (95%CI 1.175～2.841), the risk for patients with multiple punctures was higher; orally taking drugs preventing catheter thrombus, OR was 0.416 (95%CI 1.261～0.875), and the risk for patients not taking drugs was higher than that for patients taking drugs; nephropathy visit before dialysis treatment and establishing a long-term vascular access in advance were protective factors for central vein stenosis, OR were 0.319 (95%CI 0.119～0.855) and 0.162 (95%CI 0.084～0.312) respectively; left- or right-side catheterization, the OR was 0.514 (95%CI 0.268～0.986), the risk on the left was higher than the one on the right; primary disease, OR was 0.427 (95%CI 0.175～0.841), the risk for patients with diabetes mellitus was obviously higher than non-diabetic patients.

Complications according to the type of catheter: TVCs or NTHCs

There were 865 patients included in this study, in whom NTHCs were implanted 564 times, and TVCs 385 times; the monitoring times were 43051 catheter days (NTHCs) and 90758 catheter days (TVCs). Serious acute complications in the 949 total cases were rare. Only 2 patients experienced hemopneumothorax as a consequence of internal jugular vein cannulation and 1 patient experienced a hematoma due to femoral vein cannulation. All patients were fully recovered from these complications without removal of the hemodialysis catheter.

The incidence of infection related to TVCs was 5.39/1000 catheter days, and 30.29% of patients, which was lower than that of NTHCs which was 12.71/1000 catheter days, and 44.92%

of patients (both P＜0.01); incidence of catheter exit-site infection related to NTHCs was 9.15/1000 catheter days, and 39.63% of patients, higher than the rate of TVCs, which was 5.06/1000 catheter days, and 15.55% of patients (both *P*＜0.01); because NTHCs does not generate any subcutaneous tunnels thus it is hard to compare with TVCs on the incidence of subcutaneous tunnel infection, which was 2.73/1000 catheter days, and 12.87% of patients; incidence of catheter related bloodstream infections related to TVCs was 6.51/1000 catheter days, and 34.85% of patients, higher than the rate of NTHCs, which was 3.95/1000 catheter days, and was 17.48% of patients (both *P*＜0.01). The incidence of NTHCs dysfunction was 14.68/1000 catheter days, and the incidence in patients was 65.65%, higher than those of TVCs dysfunction, which was 8.64/1000 catheter days, and 44.77% of patients (both *P*＜0.01); incidence of NTHCs thrombus was 14.87/1000 catheter days, the incidence of patients was 57.72%, the incidence of NTHCs kinking or malposition was 4.41/1000 catheter days, 25.41% of patients, higher than those of TVCs which was 7.87/1000 catheter days, 38.87% of patients and 2.13/1000 catheter days, 11.0% of patients (both *P*<0.01); the incidence of TVCs fibrin shells was 2.21/1000 catheter days, 38.1% of patients, higher than that of NTHC fibrin shells, which was 1.67/1000 catheter days, 13.62% of patients (*P*=0.040 for catheter days; *P*<0.01 for patients). The incidence of TVCs central venous stenosis was 0.79/1000 catheter days, the incidence of patients was 15.28%, higher than the incidence of NTHCs, which was 0.44/1000 catheter days, 3.86% of patients (*P*=0.021 for catheter days; *P*<0.01 for patients).

Complications based on the catheter insertion site

Table 4 shows the incidence of complications with TVCs based on the catheter insertion site: In terms of catheter infection, there were no significant differences in the incidence of catheters inserted at the right internal jugular vein, left internal jugular vein, external jugular vein, and

subclavian vein (P=0.196 for catheter days; P=0.992 for patients). The incidence of thrombosis ($P<0.01$ for catheter days; P=0.017 for patients), and the incidence of malpositioned or kinked catheters (P=0.024 for catheter days; P=0.001 for patients) were higher in the left internal jugular vein than the right internal jugular vein, external jugular vein, and subclavian vein; the incidences of fibrin shells (P=0.993 for catheter days; P=0.999 for patients) were not significantly different between puncture approaches; the incidence of right internal jugular vein central venous stenosis was (P=0.036 for catheter days; P=0.004 for patients) lower than in the left internal jugular vein, external jugular vein, and subclavian vein; the incidence of femoral vein catheter infection ($P<0.01$ for catheter days; P=0.042 for patients), the incidence of thrombus ($P<0.01$ for catheter days; P=0.016 for patients) and the incidence of malpositioned or kinked catheters (P=0.036 for catheter days) were much higher than with other puncture approaches, inferior vena cava stenosis caused by femoral venipuncture was not seen.

Table 5 shows the incidence of complications with NTHCs based on catheter insertion site. For catheter infection the right internal jugular vein, left internal jugular vein, and subclavian vein (P=0.972 for catheter days; P=0.998 for patients), venous thrombosis (P=0.991 for catheter days; P=0.988 for patients) showed no significant differences; and the incidence of femoral vein (both P=0.01), and the incidence of thrombus (both P=0.01) were much higher than that of the internal jugular vein, and subclavian vein, but not lower than the incidence of fibrin shell in the femoral vein (both P=0.01); the incidence of malpositioned or kinked catheter was highest in the femoral vein ($P<0.01$ for catheter days; P=0.01 for patients), the incidence of malpositioned or kinked catheters in the left internal jugular vein was higher than those in the right internal jugular vein and subclavian vein ($P<0.01$ for catheter days; P=0.080 for patients); the incidences of (left and right side) internal jugular vein and central venous stenosis were not significantly different

(*P*=0.310 for catheter days; *P*=0.343 for patients). Femoral vein NTHCs with inferior vena cava stenosis was not seen.

Complications related to the type of catheter

The incidence of catheter type-related complications are presented in Table 6. The incidences of infection (*P*=0.976 for catheter days; *P*=0.985 for patients) and fibrin shell formation (*P*=0.963 for catheter days; *P*=1.000 for patients) related to 4 types of TVCs were not significantly different; the highest incidence of catheter thrombosis was with the use of HemoSplit and the lowest incidence was with the use of Palindrome catheters (*P*＜0.01 for catheter days;, *P*=0.002 for patients); the incidences of kinking or malposition using Permcath and Palindrome catheters were not significantly different (*P*=0.857 for catheter days; *P*=0.992 for patients), but higher than that of Cannon® Ⅱ Plus and HemoSplit catheters (*P*＜0.01 for catheter days; *P*=0.030 for patients); incidence of central venous stenosis with Cannon® Ⅱ Plus catheter was lower than with other catheters (*P*=0.025 for catheter days; *P*=0.028 for patients); Kt/V values were higher in patients using Palindrome than any of the other 3 types of TVCs, however the difference was not statistically significant (*P*=0.990).

Among the 4 types of NTHCs, the incidence of catheter infection (*P*=0.971 for catheter days; *P*=1.000 for patients) and incidence of central venous stenosis (*P*=0.963 for catheter days; *P*=0.961 for patients) were not significantly different; the incidences of thrombus (*P*=0.988 for catheter days; *P*=1.000 for patients), catheters kinking or malposition (*P*=0.991 for catheter days; *P*=0.999 for patients) and fibrin shell formation (*P*=0.997 for catheter days; *P*=0.999 for patients) were also not significantly different between the 4 types of NTHCs; Kt/V values were not significantly different between the 4 types of NTHCs (*P*=0.965).

Discussion

The objective of the present study was to investigate the incidence and risk factors of catheter-related complications in different districts and populations of Henan Province in China. The overall incidence was 7.74/1000 catheter-day or 38.61% of patients for catheter infections, 10.58/1000 catheter-day or 56.65% of patients for catheter dysfunction, and 0.68/1000 catheter-day or 8.79% of patients for central vein stenosis. Multivariate analysis showed many different factors were associated with the risk of catheter infection, catheter dysfunction and central vein stenosis.

Previous studies showed that the rate of CRI was about 3.8-6.5 per 1000 catheter-days [13, 14]. However, the rate of CRI was higher in the present study. There are a few reasons that may be responsible for this higher rate. The first are the characteristics of the patients. The patients in this study were relatively older (mean age: 49.53±18.42 years) hence were generally associated with age-related multiple organ function damage, malnutrition, impaired immunity and feebleness, all of which could increase the risk of catheter infection. Diabetes is the most frequent primary disease (27.3%), and long-term diabetes is associated with peripheral vascular disorders, preventing AVF surgery and requiring the use of catheters for dialysis. The risk of CRI was increased by 60% in patients with diabetes [15]. Patients with higher education or communication ability may be more concerned about the severity of their diseases and understand better about self-care of dialysis catheters. Urban living patients generally are highly educated than rural living ones. However, most of the patients included in the present study were from rural areas (57.5%), or with an education level of middle school or lower. Dialysis brings a heavy financial burden on patients. In the present study, most of the patients had medical

insurance from the New Rural Cooperative Medical System (44.6%) or even had no medical insurance (18.5%).

The overall infection rate in the NTHCs group was significantly higher than in the TVCs group, which is supported by previous findings [14]. Indeed, longer indwelling time might have been the main reason causing a higher rate of CRBI in the TVCs group (1052.28±371.26 days) as compared with the NTHCs group (136.2±67.4 days). Oliver et al. [14] showed that the duration of catheter indwelling was a high risk factor of CRI. Weijmer et al. [16] suggested that for patients needing NTHCs for more than 2 weeks, the catheter should be changed to TVCs to reduce the risk of infection. Longer catheter indwelling time was generally associated with low educational level of the patients (they were not fully aware of the severity of the disease). In the present study, 85.5% of the patients experienced two or more surgeries for vascular access.

Catheter dysfunction is characterized by poor blood flow. Previous studies showed that 98% of catheter dysfunctions occurring within 2 weeks were caused by either a catheter embolism or a fibrin shell [4]. Suhocki et al. [17] reported that among 163 patients with catheter dysfunctions, 74.2% had catheter embolism and 23.3% had fibrin shell. Napalkov et al. [18] performed an investigation in 3213 patients using dialysis catheters and found that the incidence of thrombosis was 8.6/1000 catheter-day. In the present study, the overall incidence rate of catheter dysfunction was 10.58/1000 catheter-day for all patients, 8.64/1000 catheter-day for placed TVCs (which was in accordance with previous studies) and 12.86/1000 catheter-day for placed NTHCs (which was substantially higher than previous studies). NTHC catheter type was a risk factor for catheter dysfunction in this study. Hyperlipidemia, arteriosclerosis, hematonosis and cancers can induce hypercoagulability [19]. In addition, patients with uremia generally have high homocysteine levels and microinflammation, which can increase thrombogenesis [19]. Too many indwelling surgeries

could damage the vascular wall, and the exposure of endothelium could promote platelet adhesion and activate endogenous coagulation pathway, which could be further aggravated by the local disturbance of hemodynamics after catheter indwelling [20]. But we did not find the times of indwelling surgery to be associated with catheter dysfunction in this study. Fibrin shells may occur in all sorts of central venous catheters, which not only induce catheter dysfunction, but also induce a series of complications including infection, thrombogenesis, catheter removal and pulmonary embolism [21, 22]. Previous studies showed that the incidence of fibrin shells was generally high. In a study performed by Oliver et al. [23], 70% of the patients with indwelled catheters were with fibrin shell. Schon et al. [24] also showed that 38% of the patients with catheter dysfunction had a fibrin shell. In the present study, the incidence rate of fibrin shell was greatly lower than in previous studies, which was 3.69/1000 catheter or 2.18% of placed catheters for the patients in the NTHCs group and 3.81/1000 catheter-day or 2.41% of placed catheters for the ones in the TVCs group. Although treatment with drugs or fibrin dissection could restore partial catheter function in some cases, there are some disadvantages including the high recurrence rate after drug-therapy and the high cost of fibrin dissection. Therefore, although several clinicians speculated that catheter dysfunction could be associated with the formation of fibrin shell, the medical cost pushed the patients to replace dialysis catheter instead of performing further imaging examinations, which underestimated the diagnostic rate of fibrin shells.

The incidence of central vein stenosis can be as high as 25%-40% [25]. Several studies also showed that 95% of the patients with central vein stenosis had a history of catheter indwelling, while only 13.6% of the patients without history of catheter indwelling developed central vein stenosis, repeated indwelling surgeries could increase the incidence of central vein stenosis in dialysis patients by 3-fold [26]. After catheter indwelling, mechanical injuries to the vascular

endothelium, secondary activation of platelet and coagulation pathways, changes in hemodynamics and extrinsic compression of catheter-surrounding tissues participated in the development of central vein stenosis [27]. Angiography is the gold standard for diagnosis of central vein stenosis [28]. In the present study, the overall incidence rate of central vein stenosis (0.68/1000 catheter-days) was relatively low, which could be due to a low diagnostic rate. Indeed, only patients with severe symptoms (including severe facial swelling, limb swelling, limb pain, and intracranial hypertension) were examined by angiography, while most patients without symptoms or only with mild symptoms were not diagnosed due to high medical costs or insufficient awareness from the clinicians. The incidence was significantly higher in patients using TVCs (0.79/1000 catheter-days) compared those with NTHCs (0.44/1000 catheter-days, $P<0.05$), which might be associated with the stimulations to the vascular wall caused by the long duration of TVCs indwelling. Diabetes is an important risk factor for central vein stenosis, which could be caused by long-term influences of high glucose, chronic inflammation, and lipid metabolism disorders, increasing the risk of angiosclerosis, vascular wall thickening, reduced elasticity, thrombogenesis and stenosis in diabetic patients on dialysis [29].

In this study, four different types of TVCs and four different types of NTHCs were used in the 14 participating hospitals. Since no specific coating was applied to each of the four types of TVCs to prevent infection and thrombosis, and since the indwelling duration of these four types of TVCs was similar, no significant difference in the incidence rate of catheter infection was found among these four types of TVCs. However, the incidence of catheter embolism was significantly higher with the HemoSplit™ catheter compared with the other types, and the incidence of catheter embolism in patients using the Palindrome™ catheter was the lowest, which could be associated with different designs of the side holes at the tip of the catheters. The

side holes in Palindrome™ catheter are relatively large rectangles made by laser notching, which are relatively difficult for thrombi to adhere to [30], while the side holes in the HemoSplit™ catheter are relatively small round holes that could be easily adhered by thrombi. The texture and cuff rings are identical in the Palindrome™ and Permcath™ catheters, of which the rates of catheter kinking and malposition were significantly higher compared with the other two types of TVCs. The specific "retrograde design" of the Cannon II Plus catheter [31] makes sure that the cuff ring is fixed to the clavicle, while the cuff ring in the HemoSplit™ catheter can be closely connected with the adjacent tissues. Therefore, these two catheters had a lower risk of kinking and malposition. The incidence rate of central vein stenosis with the Cannon II Plus™ catheter was the lowest among all the four types of TVCs, which could be associated with the tip of the catheter that was placed in the right atrium so that the stimulation to the superior vena cava was relatively small. There were no significant differences in the incidence of any complications between the four different NTHCs used in this study.

These results suggest that healthcare policies for patients with CKD should be modified, for example we suggest the following points: 1. Arrange for a nephrosis specialist to interview the early stage CKD patient periodically, and educate the patient about hemodialysis and vascular access; 2. Formulate strict early referral procedure, to avoid delayed diagnosis and treatment of end stage renal disease (ESRD) due to lack of expertise of GPs; 3. Health administrative departments should evaluate the quality of hemodialysis based on the ratio of patients with catheter in their hemodialysis centers; 4. Hemodialysis centers should set up a vascular access team which consists of a nephrosis specialist, hemodialysis experts, hemodialysis nurse specialist, vascular surgeon, interventional therapy doctor, and caretaker to better maintain the lifeblood of the maintenance hemodialysis (MHD) patient.

This present study has several limitations. First, there remains residual confounding from unmeasured variables such as medical therapy, nutritional status of the patients, biochemical indexes and psychosocial factors. Second, Henan Province covers a large area and has a large population, and the levels of economics, culture and healthcare vary greatly among different districts. Since all 14 participating hospitals included were from the districts with relatively high economic level, the epidemiological features of catheter-related complications could be different from remote areas or other districts with relatively low economic level. Therefore, the incidence of catheter-related complications could be underestimated in the present study.

In conclusion, patients receiving dialysis in Henan Province had a high rate of dialysis catheter use with long duration of temporary catheter indwelling, which resulted in a high incidence of catheter-related complications. Therefore, the healthcare administration should develop policies to assess patients early, ideally prior to the requirement for dialysis, to allow preparation in advance to establish permanent vascular access as soon as possible.

Authors' contributions

KW and ZSL have made substantial contributions to conception and design; KW, PW, XHL, XQL and ZSL have made substantial contributions to acquisition of data, or analysis and interpretation of data; KW and ZSL has been involved in drafting the manuscript or revising it critically for important intellectual content; all authors have given final approval of the version to be published.

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Competing interests

The authors declare that they have no competing interests.

Data sharing statement

Technical appendix, statistical code and dataset are available from the corresponding author at the Dryad repository, which will provide a permanent, citable and open access repository for the dataset.

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Table 1. Patient characteristics

Characteristics	**Values** (N=865)
NTHCs	564
TVCs	385
Indwelling time (days)	
NTHCs	136.2±67.4
TVCs	1052.3±371.3
Permanent catheter	
Quinton Palindrome™	103 (24.4%)
Quinton Permcath™	91 (21.6%)
Arrow Cannon II Plus™	101 (29.1%)
Bard HemoSplit™	90 (24.9%)
Age (years)	49.53±18.42
≤18	126 (14.6%)
19-44	212 (24.5%)
45-59	236 (27.3%)
≥60	291 (33.6%)
Gender	
Male	495 (57.2%)
Female	370 (42.8%)
Marital status	
Married	487 (56.3%)
Single	285 (32.9%)
Widowed or divorced	93 (10.8%)
Education	
University	152 (17.6%)
Middle school	481 (55.6%)
Below primary school	232 (26.8%)
Occupation	
Farmer	352 (40.7%)
Worked	124 (14.3%)
Office worker	95 (11.0%)
Retired	165 (19.1%)
Unemployed	129 (14.9%)
Registered residence	
Rural	497 (57.5%)
Urban	368 (42.5%)
Medical costs	
New Rural Cooperative Medical System	386 (44.6%)
Medical insurance	319 (36.9%)
Self-paying	160 (18.5%)
Primary disease	
Diabetic kidney disease	236 (27.3%)
Primary nephropathy	143 (16.5%)
Hypertensive nephropathy	96 (11.1%)

Acute renal failure	44 (5.1%)
Obstructive nephropathy	72 (8.3%)
Renal tubular interstitial disease	62 (7.2%)
Drug-induced renal damage	39 (4.5%)
Myeloma	24 (2.8%)
Others	103 (11.9%)
Hemodialysis duration, median (range)	26.5 months (15 day-18 years)
Hemodialysis frequency	
Twice per week	375 (43.4%)
Three times per week	182 (21.0%)
Three times per two weeks	121 (14.0%)
Five times per two weeks	145 (16.8%)

Table 2. Univariate logistic regression of factors influencing the development of dialysis catheter-related complications

Variables	Catheter-infection			Catheter dysfunction			Central vein stenosis		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age	0.427	0.242-0.631	0.041	1.157	0.745-1.797	0.516	1.469	0.934-2.310	0.096
Gender	0.752	0.491-1.152	0.19	1.046	0.680-1.610	0.837	1.132	0.723-1.772	0.588
Primary disease	0.416	0.262-0.826	< 0.01	0.738	0.266-1.613	0.125	0.692	0.148-0.871	< 0.01
Marriage	1.109	0.701-1.754	0.658	1.318	0.819-2.122	0.256	1.377	0.854-2.221	0.189
Education									
University			< 0.01			0.225			0.150
Middle school	0.669	0.406-1.104	0.116	0.668	0.411-1.086	0.104	0.669	0.406-1.104	0.116
Below primary school	2.405	1.373-4.214	0.002	0.962	0.538-1.719	0.895	0.392	0.204-0.753	0.072
Occupation	1.380	0.892-2.136	0.148	1.151	0.743-1.783	0.528	1.333	0.838-2.121	0.224
Registered residence	0.250	0.157-0.398	< 0.01	0.218	0.137-0.345	< 0.01	0.352	0.217-0.571	0.092
Medical costs									
New Rural Cooperative Medical System			0.315			0.032			0.546
Medical insurance	1.475	1.273-2.138	0.076	3.762	0.517-6.319	0.047	1.545	0.612-1.941	0.239
Self-paying	1.958	0.512-2.731	0.089	6.412	3.309-12.076	0.017	1.368	0.203-1.628	0.202
Frequency of dialysis	0.882	0.735-1.059	0.180	0.905	0.750-1.092	0.296	0.937	0.772-1.136	0.507
Duration of hemodialysis	1.716	0.782-3.769	0.178	1.703	0.700-4.144	0.240	3.073	1.387-6.807	0.063
Nephropathy visit before dialysis treatment	0.110	0.064-0.189	< 0.01	0.056	0.033-0.097	< 0.01	0.249	0.148-0.420	< 0.01
Pre-established permanent vascular access	0.242	0.154-0.381	< 0.01	0.114	0.063-0.208	< 0.01	0.225	0.140-0.362	< 0.01
Catheter type	0.654	0.425-1.005	0.052	1.793	1.510-2.231	0.031	1.082	0.685-1.708	0.736
Catheter position	0.521	0.338-0.804	0.603	0.067	0.034-0.130	< 0.01	0.325	0.204-0.516	< 0.01
Number of indwelling surgeries	1.148	0.888-1.485	0.292	1.669	1.276-2.183	0.086	2.471	1.818-3.360	< 0.01
Imaging	2.720	1.696-4.363	0.728	2.827	1.804-4.430	<	2.106	0.148-0.420	0.083

examination after catheter implantation						0.01			
Catheter puncturing approach vessels									
Femoral vein			0.227			< 0.01			0.110
Internal jugular venous	0.835	0.460-1.516	0.554	0.126	0.044-0.361	< 0.01	0.37	0.202-0.678	0.172
External jugular vein	0.363	0.126-1.047	0.061	0.060	0.017-0.216	< 0.010	0.355	0.128-0.984	0.471
Subclavian vein	0.572	0.219-1.495	0.255	0.094	0.027-0.332	< 0.01	0.321	0.117-0.882	0.282
Taking drugs preventing catheter thrombus orally	0.218	0.125-0.379	< 0.01	0.100	0.059-0.168	< 0.01	0.189	0.089-0.362	< 0.01
Hemoglobin	0.400	0.300-0.534	0.061	1.421	1.318-1.558	< 0.01	0.514	0.383-0.689	0.078
Albumin	0.151	0.102-0.224	< 0.01	0.369	0.278-0.489	0.572	0.585	0.441-0.777	0.347
Ferritin	1.857	1.375-2.508	< 0.01	0.96	0.717-1.286	0.786	0.898	0.663-1.218	0.49

Table 3. Multivariate logistic regression of factors influencing the development of dialysis catheter-related complications

Independent variables	OR	95% CI	*P* Value
Catheter infection			
Age	0.351	0.136-0.674	0.006
Registered residency	0.25	0.12-0.52	<0.01
Primary disease	0.379	0.176-0.818	0.013
Education degree	0.334	0.198-0.565	<0.01
University			<0.01
Middle school	1.224	0.547-2.736	0.623
Below primary school	10.757	3.637-31.817	<0.01
Nephropathy visit before dialysis treatment	0.22	0.096-0.502	<0.01
Establishing long-term vascular access in advance	0.401	0.193-0.832	0.014
Taking drugs preventing catheter thrombus orally	0.611	0.404-0.923	0.019
Albumin	0.142	0.085-0.237	<0.01
Ferritin	2.162	1.412-3.308	<0.01
Catheter dysfunction			
Registered resident	0.21	0.045-1.013	<0.01
Taking drugs preventing catheter thrombus orally	0.106	0.041-0.274	<0.01
Imaging examination after catheter implantation	2.631	1.293-5.354	0.008
Catheter type	3.493	1.358-8.983	0.009
Medical costs			
Medical insurance			0.004
New Rural Cooperative Medical System	0.949	0.265-3.403	0.936
Self-paying	13.416	2.541-70.827	0.002
Nephropathy visit before dialysis treatment	0.048	0.018-0.124	<0.01
Establishing long-term vascular access in advance	0.025	0.006-0.109	<0.01
Catheter left or right	0.024	0.007-0.080	<0.01
Catheter puncturing approach vessels			
Femoral vein			<0.01
Internal jugular venous	0.029	0.005-0.179	<0.01
External jugular vein	0.011	0.001-0.089	<0.01
Subclavian vein	0.015	0.002-0.125	<0.01
Hemoglobin	2.276	1.101-4.749	0.012
Central vein stenosis			
Catheterized surgery times	1.827	1.175-2.841	0.007
Taking drugs preventing catheter thrombus orally	0.416	0.261-0.875	0.043
Nephropathy visit before dialysis treatment	0.319	0.119-0.855	0.023
Establishing long-term vascular access in advance	0.162	0.084-0.312	<0.01
Left- or right- catheterization	0.514	0.268-0.986	0.045
Primary disease	0.427	0.175-0.841	0.007

Table 4. Morbidity of complications related to TVCs

Catheter-related complications			TVCs				
			Right internal jugular venous	Left internal jugular venous	Femoral vein	External jugular vein	Subclavian vein
Infection	Exit-site infection	(%)	14.35	15.31	37.5	16	16.22
		times/1000 catheter day	4.93	5.06	10.68	5.26	5.16
	Tunnel infection	(%)	11.96	13.27	18.75	12	13.51
		times/1000 catheter day	2.76	2.68	3.56	2.72	2.75
	CRBI	(%)	34.45	34.70	43.75	36	35.14
		times/1000 catheter day	6.69	6.49	10.08	6.62	6.42
Dysfunction	Thrombus	(%)	39.71	58.16	62.5	40	37.84
		times/1000 catheter day	7.96	13.94	14.83	7.81	7.68
	Fibrin shell	(%)	38.76	37.76	37.5	36	37.84
		times/1000 catheter day	2.15	2.03	2.08	2.21	2.29
	Malposition or kinking	(%)	11.48	29.51	43.75	12	13.51
		times/1000 catheter day	2.07	3.25	3.26	2.21	2.19
Central venous stenosis		(%)	12.44	27.55	0	28	27.03
		times/1000 catheter day	0.59	1.17	0	1.19	1.15

Note: fibrin shell and Central venous stenosis need to be proofed via imaging examination before being taken into statistical analysis.

Table 5. Morbidity of NTHC related complications

Catheter-related complications			NTHCs			
			Right internal jugular venous	Left internal jugular venous	Femoral vein	Subclavian vein
Infection	Exit-site infection	(%)	36.7	36.2	48.37	35.48
		times/1000 catheter day	8.79	8.54	19.66	8.85
	Tunnel infection	(%)	/	/	/	/
		times/1000 catheter day	/	/	/	/
	CRBI	(%)	16.51	17.39	29.77	17.74
		times/1000 catheter day	3.57	3.61	9.93	3.75
Dysfunction	Thrombus	(%)	58.7	59.42	78.6	58.06
		times/1000 catheter day	14.74	15	29.98	14.79
	Fibrin shell	(%)	13.76	14.49	4.19	14.53
		times/1000 catheter day	1.53	1.9	0.39	1.69
	Malposition or kinking	(%)	24.31	37.68	45.12	24.19
		times/1000 catheter day	4.37	10.06	19.86S	4.86T
Central venous stenosis		(%)	3.67	4.35	0	8.06
		times/1000 catheter day	0.45	0.27	0	0.62

Table 6. Morbidity of types of catheter related complications

Catheter-related complications			TVC types			NTHC types				
			Palindrome™	Permcath™	Cannon® II Plus	HemoSplit™	ARROW	DIALL	ABEL	TYCO
Infection	Exit-site infection	(%)	15.69	15.38	15.24	16.09	36.08	36.2	35.97	35.58
		times/1000 catheter day	5.12	5.08	4.97	5.17	8.96	9.08	9.05	8.82
	Tunnel infection	(%)	12.75	13.19	12.38	13.79	/	/	/	/
		times/1000 catheter day	2.74	2.7	2.75	2.83	/	/	/	/
	CRBI	(%)	35.29	35.16	35.24	35.63	17.09	17.18	17.27	17.31
		times/1000 catheter day	6.53	6.43	6.5	6.68	3.48	3.54	4.05	3.65
Catheter dysfunction	Thrombus	(%)	22.55	38.46	39.05	49.42	57.59	57.67	57.55	57.69
		times/1000 catheter day	5.32	8.76	7.31	9.8	15.01	15.03	14.51	14.86
	Fibrin shell	(%)	38.24	38.46	38.1	37.93	13.92	14.11	13.67	13.46
		times/1000 catheter day	2.25	2.06	2.1	2.07	1.49	1.53	1.6	1.51
	Malposition or kinking	(%)	18.63	18.68	8.57	10.34	31.01	30.67	30.22	30.77
		times/1000 catheter day	2.73	2.66	1.47	1.51	8.54	8.52	8.29	8.19
Central venous stenosis		(%)	14.71	15.38	3.81	14.94	3.8	4.91	4.32	3.85
		times/1000 catheter day	0.75	0.84	0.24	0.88	0.5	0.64	0.57	0.5
Kt/V			1.40±0.73	1.39±0.19	1.38±0.13	1.38±0.17	1.06±0.07	1.05±0.07	1.06±0.13	1.06±0.08

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8, 10-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8, 10-11
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	12
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	12
		(*b*) Describe any methods used to examine subgroups and interactions	12
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	12
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	13
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-13
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13-18
		(*b*) Report category boundaries when continuous variables were categorized	13-15
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	21
Discussion			
Key results	18	Summarise key results with reference to study objectives	21-22
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	26-27
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	22-26
Generalisability	21	Discuss the generalisability (external validity) of the study results	27
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	28

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.