Tunnelled haemodialysis catheter and haemodialysis outcomes: a retrospective cohort study in Zagreb, Croatia

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ABSTRACT

Objectives: Studies have reported that the tunnelled dialysis catheter (TDC) is associated with inferior haemodialysis (HD) patient survival, in comparison with arteriovenous fistula (AVF). Since many cofactors may also affect survival of HD patients, it is unclear whether the greater risk for survival arises from TDC per se, or from associated conditions. Therefore, the aim of this study was to determine, in a multivariate analysis, the long-term outcome of HD patients, with respect to vascular access (VA).

Design: Retrospective cohort study.

Participants: This retrospective cohort study included all 156 patients with a TDC admitted at University Hospital Merkur, from 2010 to 2012. The control group consisted of 97 patients dialysed via AVF. The groups were matched according to dialysis unit and time of VA placement. The site of choice for the placement of the TDC was the right jugular vein. Kaplan-Meier analysis with log-rank test was used to assess patient survival. Multivariate Cox regression analysis was used to determine independent variables associated with patient survival.

Primary outcome measures: Patient survival with respect to VA.

Results: The cumulative 1-year survival of patients who were dialysed exclusively via TDC was 86.4% and of those who were dialysed exclusively via AVF, survival was 97.1% (p=0.002). In multivariate Cox regression analysis, male sex and older age were independently negatively associated with the survival of HD patients, while shorter HD vintage before the creation of the observed VA, hypertensive renal disease and glomerulonephritis were positively associated with survival. TDC was an independent risk factor for survival of HD patients (HR 23.0, 95% CI 6.2 to 85.3).

Conclusion: TDC may be an independent negative risk factor for HD patient survival.

INTRODUCTION

The number of patients with end-stage renal disease (ESRD) in need of renal replacement therapy increases progressively in Europe and worldwide.1 This puts chronic kidney disease (CKD) among the significant factors of morbidity and mortality, and represents a growing public health issue.

In patients on haemodialysis (HD) treatment, possible long-term vascular access (VA) types are: arteriovenous fistula (AVF), arteriovenous graft (AVG) and tunnelled HD central venous catheter (TDC). Since native AVF, described by Brescia and Cimino in 1966, has the longest survival and the lowest frequency of complications among all other types of VA for HD, it should be the first choice for VA whenever possible.1–3 However, there are vast differences in the use of certain VA types in different countries and the use of TDC is still noticeably high, in spite of current guidelines. The rate of patients who are dialysed via TDC among all patients on HD varies from only 1.6% in Japan up to 52% in Canada.4 In Croatia, ~20% of patients are dialysed via TDC, while the rest are dialysed via AVF (M Knotek, personal communication, 2015). AVG is infrequently used in Croatia.

Strengths and limitations of this study

- This is a retrospective cohort study in which well matched patients followed by multiple dialysis centres were included. Therefore, study results account for variations in routine patient care at different centres and are reflective of real-life practice. This is important, because a prospective randomised trial comparing patient survival with respect to vascular access type (arteriovenous fistula and tunnelled dialysis catheter) is highly unlikely.
- Main outcomes (patient and vascular access survival) were analysed by multivariate analysis.
- The main limitation of this study is its retrospective and non-randomised design. However, the two patient groups were well matched in the majority of variables that may have affected the outcome.
Central venous catheters (CVCs) are used for the rapid establishment of adequate VA when there is an urgent need for HD, as a bridge during AVF maturation process and in patients who have eventually exhausted all other VA types. According to the kidney disease outcomes quality initiative (K/DOQI) guidelines, temporary catheters should be used for up to 1 week, while the use of TDC is recommended in all other cases where catheter use is unavoidable. TDCs are usually placed through the subclavian or femoral vein. The subclavian vein should generally be avoided because of the high incidence of stenosis and thrombosis, while the femoral vein should be considered only when all other insertion sites have been excluded. The advantages of the TDC include the ability to use it immediately after placement, no repeated venipuncture and no haemodynamic consequences, and no need for a vascular surgeon during placement. Nevertheless, TDCs are associated with significantly higher long-term risk of death, infections, cardiovascular events and hospitalisation in comparison with other VA types. However, at the same time, some of the associated conditions and diseases affect patient survival, as well as VA choice and survival. Therefore, although many studies show that TDCs are associated with poorer patient survival, it is not entirely clear whether the risk arises from the TDC exclusively, or from the associated conditions and diseases that are often present in patients who are dialysed via TDC.

The aim of this study was to determine HD patient and VA survival with respect to VA type.

PATIENTS AND METHODS

Patients

This retrospective cohort study was approved by the Hospital Ethics Committee of the University Hospital Merkur, Zagreb, Croatia. Patients gave their written informed consent for anonymised HD data collection for research purposes. We analysed the survival of patients dialysed via a TDC in comparison with a group of patients who were dialysed via an AVF. We also analysed TDC survival. The study included a total of 253 patients who were treated with HD in 21 dialysis centre in Croatia; median 16 (IQ, 10, 21) per centre. With respect to VA, the TDC:AVF ratio was approximately 2:1. The study subjects were selected to include all 156 patients who received a total of 190 TDC at the Renal Division in University Hospital Merkur, from the beginning of 2010 to the end of 2012. Then, 97 patients who were dialysed via AVF were selected from the same dialysis centres. Eligible patients dialysed via AVF had to start with HD treatment at about the same time as patients dialysed via TDC. The insertion site of choice for the TDC was the right jugular vein. Other sites were used in case of inability to use the right jugular vein or when exchanging over a previously inserted TDC in another vein. All TDCs were manufactured by Medcomp Inc (Harleysville, Pennsylvania, USA). For an internal jugular and subclavian approach, either SST28SE or SST32SE catheters were used, while SST40SE catheters were used for a femoral approach. All catheters were 14 Fr.

Methods

Data were collected from the Renal Division TDC placement programme database and by a questionnaire sent to the 21 HD centres where patients underwent TDC placement procedure in our division. In the questionnaire, we asked for the following information: demographic data, the date of first HD, history of a temporary CVC before the observed TDC, history of an attempt to create an AVF or history of a functional AVF that ceased to function, the cause of CKD, concomitant diseases, history of catheter sepsis, history of an infection of the TDC tunnel, whether there were problems with wound healing after TDC placement, whether there were mechanical problems with the TDC and what solution the TDC problem was usually solved with on the completion of HD treatment. If the TDC was functional, information on the blood pump speed, and on arterial and venous pressure during HD treatment, was inquired about. If TDC ceased to function, we recorded the date of cessation of TDC function, the reason for cessation of TDC function, current VA if the patient was still treated with HD, the date of transplantation if the patient underwent a kidney transplantation and the date of death if the patient died. A similar, modified questionnaire was used to collect data about patients who were dialysed via AVF.

Statistical analysis

Numerical data are presented as mean±SD in case of continuous variables with normal distribution or as median with IQR in case of non-normal distribution. The difference between two groups regarding continuous variables was tested with Student’s t test in normal distributed variables or with Mann-Whitney’s χ² test. Survival analysis, which included patient survival, overall VA survival and death-censored VA survival, was performed using Kaplan-Meier analysis. Univariate and multivariate Cox regression were performed to determine variables independently associated with patient and VA survival. All variables that were associated with respective outcome in bivariate analysis (at p<0.1) were included in the multivariate Cox regression. Results are presented as HR with the corresponding 95% CI. Statistical significance was considered at p value <0.05. All statistical analyses were performed using SPSS V.17.0.

RESULTS

Characteristics of patients dialysed via TDC

Patient characteristics are shown in table 1. There were 156 patients dialysed via TDC. The cause of ESRD was
Patient survival is shown in figure 1A. Cumulative 1-year overall patient survival since the initiation of HD treatment was 99.2%. In univariate analysis of risk factors for the overall patient survival, there were eight negative risk factors: TDC as current VA (p=0.001), TDC as an exclusive VA (p=0.001), male gender (p=0.0065), older age at the initiation of HD treatment (p=0.006), concomitant diabetes mellitus (p=0.021), stroke in patient’s history (p=0.028), concomitant coronary heart disease (p=0.017) and prior peripheral artery revascularisation (p=0.028). Factors positively associated with overall patient survival were shorter HD vintage prior to the observed VA (p=0.004) and an attempt to create an AVF or history of an AVF that ceased to function prior to the current VA (p=0.037). With respect to ESRD, hypertensive renal disease (p=0.001) and glomerulonephritis (p=0.002) were positively associated with overall patient survival. The results of univariate analysis are shown in table 2. In the multivariate Cox regression, two factors turned out as independent negative risk factors for overall patient survival: male gender (p=0.012) and older age at the initiation of HD treatment (p=0.037). Shorter HD vintage prior to the observed VA (p<0.001), hypertensive renal disease (p=0.002) and glomerulonephritis (p=0.018) were independently positively associated with overall patient survival. TDC was independently negatively associated with patient survival in the multivariate analysis (HR 23.0, 95% CI 6.2 to 85.3).

Patient survival with respect to VA is shown in figure 1B. Cumulative 1-year survival of patients who were dialysed exclusively via TDC was 91.2% and of those who were dialysed exclusively via AVF, 97.1% (p=0.001). With respect to VA conversion, 1-year survival of patients who were converted from TDC to AVF was 95% (p=0.102 in comparison with TDC as an exclusive VA; p=0.002 in comparison with TDC as an exclusive VA).

In univariate analysis of risk factors for the survival of patients who were dialysed exclusively via TDC, there were four negative risk factors: male gender (p=0.010), concomitant diabetes mellitus (p=0.006), concomitant coronary artery disease (p=0.004) and prior peripheral artery revascularisation (p=0.003). Factors positively associated with survival were shorter HD vintage prior to the current VA (p<0.001), an attempt to create an AVF or an AVF that ceased to function prior to the current VA (p=0.001), hypertensive renal disease (p=0.001) and glomerulonephritis (p=0.006). The results of univariate analysis are shown in table 2. In the multivariate Cox regression, only male gender turned out as an independent negative risk factor (p=0.019), while shorter HD vintage prior to the current VA (p<0.001), an attempt to create an AVF or an AVF that ceased to function prior to the current VA (p=0.039) and hypertensive kidney disease as the cause of ESRD were independently positively associated with survival.

### Table 1 Characteristics of patients

|                          | All patients | TDC       | AVF       | p Value |
|--------------------------|--------------|-----------|-----------|---------|
| Age of patients at initiation of HD treatment (years)* | 62.7±14.0    | 62.1±14.4 | 63.9±13.2 | 0.215   |
| Age of patients at VA creation (years)*               | 63.8±13.9    | 63.7±14.2 | 64.0±13.4 | 0.737   |
| Age of patients at end of follow-up (years)*          | 65.8±13.9    | 65.2±14.3 | 66.9±12.9 | 0.248   |
| Sex (male/female)       | 152/101      | 88/68     | 64/33     | 0.081   |
| HD vintage (days)†       | 607 (335, 1088) | 658 (374, 1114) | 536 (320, 1139) | 0.836   |
| HD vintage before observed VA creation (days)†        | 50 (5, 348)  | 204 (33, 799) | 7 (0, 66)  | <0.001  |
| Diabetes mellitus        | 42.7%        | 44.2%     | 40.2%     | 0.464   |
| Coronary heart disease   | 20.6%        | 20.5%     | 20.6%     | 0.851   |
| Stroke                   | 11.9%        | 16.7%     | 4.1%      | 0.001   |
| Peripheral vascular disease| 20.2%       | 19.9%     | 20.6%     | 0.902   |
| Peripheral artery revascularisation | 6.3%   | 6.4%     | 6.2%      | 0.228   |
| Partial or total limb amputation | 14.2% | 15.4%     | 12.4%     | 0.599   |

*Mean±SD.
†Median with IQR.
AVF, arteriovenous fistula; HD, haemodialysis; TDC, tunnelled haemodialysis catheter; VA, vascular access.
VA survival

Among the total of 190 TDCs, 124 (65.3%) were placed de novo. Altogether, 58% of TDCs were placed in the right jugular vein, 11.2% in the left jugular vein, 17.6% in the right subclavian vein, 8.5% in the left subclavian vein, 2.7% in the right femoral vein and 2.1% in the left femoral vein. The most frequent long-term complications were TDC thrombosis and infection; 6.8% of infections led to TDC-associated sepsis and 6.3% were tunnel infections. Of these, 35.3% of infections were cured without catheter removal. The TDC was replaced in 47.1% of infection cases and permanently removed in 5.9% of cases. Of the infections, 11.8% ended in a lethal outcome. The wound healing problems after TDC placement occurred in 5.8% of patients. Mechanical problems (rupture or separation of catheter lines, puncture or rupture of the clamp or cap) were reported in 7% of cases. The mean blood pump speed for TDCs in use was 288±36 mL/min, mean pressure in the venous line of the dialysis machine was 158±35 mm Hg while mean pressure in the arterial line was −184±39 mm Hg. TDCs were closed with sodium citrate (Duraloc) exclusively in 20.3% of cases, and in 67.4% cases, with heparin exclusively, the rest were closed either with sodium citrate or with heparin. During HD treatment it was necessary to switch TDC lines every time in 10.5% of TDCs, occasionally in 27.4%. During this monitoring process, 50% of TDCs ceased to function. The causes of cessation are shown in table 3.

TDC death-censored survival is shown in figure 2. One-year death-censored TDC survival was 76.7%. In univariate analysis, there were four risk factors negatively associated with TDC survival: an attempt to create an AVF or an AVF that ceased to function prior to the current VA (p=0.010), TDC-associated sepsis (p<0.001), tunnel infection (p<0.001) and mechanical problems with TDCs (p<0.001). In the multivariate Cox regression, an attempt to create an AVF or an AVF that ceased to function prior to the current VA (p=0.014), mechanical problems with the TDC (p=0.002) and TDC line puncture or rupture (p=0.001) were independently negatively associated with TDC death-censored survival.

The mean blood pump speed for AVF in use was 318 ±36 mL/min, mean pressure in the venous line of the dialysis machine was 137±32 mm Hg, while mean pressure in the arterial line was −154±37 mm Hg. During this monitoring process, 13.4% of AVFs ceased to function. The causes of cessation are shown in table 4.

AVF death-censored survival is shown in figure 2. One-year death-censored AVF survival was 96%. In univariate analysis, male gender was negatively associated with AVF death-censored survival (p=0.004). No variable was independently associated with death-censored AVF survival in multivariate Cox regression.

VA death-censored survival (both TDC and AVF) is shown in figure 2. In univariate analysis, there were three factors negatively associated with VA death-censored survival: TDC as VA type (p<0.001), an attempt to create an AVF or an AVF that ceased to function prior to the observed VA (p<0.001) and TDC as an exclusive VA (p<0.001). In multivariate Cox regression, AVF as an exclusive VA was independently positively associated with VA survival (p<0.001).

DISCUSSION

This analysis defined factors associated with VA and patient survival in a real-life situation, in a patient population treated in 21 dialysis centres across Croatia. The cause of ESRD in a studied group of patients completely

Figure 1 (A) Kaplan-Meier curve for overall HD patient survival. HD, haemodialysis (B) Kaplan-Meier curve for HD patient survival with respect to vascular access. AVF, arteriovenous fistula, TDC, tunnelled haemodialysis catheter; VA, vascular access.
coincided with Croatian Registry of Renal Replacement Therapy data. The frequency of concomitant diseases was similar to that in other developed countries. One-year patient survival in this study was excellent, probably reflecting good HD care in Croatia. Female gender was independently positively associated with overall patient survival. This was previously shown in the Choices for Healthy Outcomes in Caring for ESRD study by Astor et al., where TDC as current VA, male gender and older age at initiation of HD treatment were independently negatively associated with overall patient survival.

In a recent cohort study of 3752 dialysis patients, 1-year survival of patients who were dialysed via TDC was 75% and factors independently negatively associated with survival were age at first treatment, late referral, coronary artery disease, peripheral vascular disease and cerebrovascular disease. One-year survival of patients dialysed via AVF was 90%.

Table 2 Patient survival—the results of univariate and multivariate analysis

| VA type          | 1-year survival (%) | 2-year survival (%) | p Value | HR (95% CI) | p Value |
|------------------|---------------------|---------------------|---------|-------------|---------|
| TDC              | 91.2                | 77.7                | 0.001*  | 3.8 (1.6 to 8.9) | 0.002   |
| AVF              | 97.2                | 95.7                |         |             |         |
| Sex              |                      |                     |         |             |         |
| Male             | 91.1                | 79.0                | 0.065*  | 1.7 (0.9 to 3.2) | 0.069   |
| Female           | 96.5                | 89.0                |         |             |         |
| An attempt to create an AVF or an AVF that ceased to function prior to the observed VA | Yes | 95.7 | 87.4 | 0.037* | 1.8 (1.1 to 3.1) | 0.040 |
|                  | No                  | 91.3                | 78.6                |         |         |
| Concomitant diabetes mellitus | Yes | 91.2 | 76.7 | 0.021* | 0.5 (0.3 to 0.9) | 0.023 |
|                  | No                  | 94.8                | 87.5                |         |         |
| Stroke in patient’s history | Yes | 94.6 | 72.9 | 0.028* | 0.5 (0.3 to 0.9) | 0.031 |
|                  | No                  | 93.0                | 84.9                |         |         |
| Concomitant coronary heart disease | Yes | 93.2 | 68.9 | 0.017* | 0.5 (0.3 to 0.9) | 0.019 |
|                  | No                  | 93.3                | 88.2                |         |         |
| Peripheral artery revascularisation | Yes | 100 | 57.9 | 0.028* | 0.5 (0.2 to 0.9) | 0.033 |
|                  | No                  | 92.7                | 86.2                |         |         |
| VA conversion    |                      |                     |         |             |         |
| A                | 86.4                | 64.8                | <0.001* | 2.8 (1.5 to 5.0) | 0.001   |
| B                | 97.1                | 95.5                |         |             |         |
| C                | 95.0                | 86.5                |         |             |         |
| Hypertensive kidney disease | Yes | 96.0 | 96.0 | <0.001* | 0.2 (0.1 to 0.5) | 0.002 |
| Glomerulonephritis | 100                 | 100                 | <0.001* | 0 (0 to 0.3) | 0.018 |
| The age of patients at the initiation of HD treatment (years) | 1.0 (1 to 1.1) | 0.037 |
| Time from the initiation of HD treatment to the observed VA creation (months) | 0.8 (0.7 to 0.9) | 0.006 |

Table 3 Causes of TDC function cessation

| Cause                                      | N (%) |
|--------------------------------------------|-------|
| Death of a patient                         | 37 (43.0) |
| TDC thrombosis                             | 14 (16.3) |
| TDC infection                              | 9 (10.5) |
| VA conversion from TDC to AVF              | 8 (9.3) |
| Kidney transplantation                      | 6 (7.0) |
| Recovery of renal function                  | 2 (2.3) |
| Catheter fell out                           | 1 (1.2) |

AVF, arteriovenous fistula; HD, haemodialysis; TDC, tunnelled haemodialysis catheter; VA, vascular access.
Kaplan-Meier curve for vascular access death-censored survival. AVF, arteriovenous fistula; TDC, tunnelled haemodialysis catheter; VA, vascular access.

Figure 2

with previously published studies. Several studies showed that patient survival is associated with VA conversion and is better in patients who are converted from TDC to AVF during the first year of HD treatment.10 15 Although our study did not include enough patients who underwent this kind of VA conversion analysis, we showed that survival was not significantly different in patients who were dialysed exclusively via VA and those who were converted from AVF to TDC. Therefore, it is likely that there are other factors besides TDC that are responsible for lower survival of patients dialysed exclusively via TDC. Multivariate Cox regression showed that VA type is an independent risk factor for patient survival. The association of VA type with patient survival is controversial. Multiple studies, including ours, suggested negative correlation between TDC and patient survival.9 10 12 14 16 On the other hand, according to several retrospective studies, TDC per se may not be negatively associated with poor patient survival.17 18 This issue could be clarified only by prospective randomised control studies, which are difficult to perform.

Studying the association of TDCs with HD patient outcomes is important, because the number of patients who are dialysed via TDC is steadily increasing.19 20 A ~20% of dialysis patients in Croatia are dialysed via TDC (M Knotek, personal communication). Although K/DOQI guidelines recommend that <10% of all patients treated with HD should be dialysed via TDC, this goal remains unachieved.20 The number of patients who initiate HD treatment via TDC is also much higher than recommended.19 Possible reasons are late referral to a nephrologist, a lack of surgeon availability for AVF creation and an increasing proportion of elderly patients who are not eligible for AVF creation due to their poor blood vessel status.21

In one British study of 812 TDC, 1-year death-censored TDC survival of 61% was demonstrated.22 Another study of 200 Tesio catheters reported a 1-year death-censored catheter survival of 60%.23 Our results show significantly better 1-year TDC survival, in comparison with these previously published studies. According to guidelines, the right jugular vein was the insertion site of choice at our centre, but this study did not find a statistically significant difference between the insertion site and TDC survival (data not shown). This may be due to the low power of the study for this analysis, as number of TDC insertions at other sites was low.

In conclusion, we found in the present study that the TDC may be an independent negative risk factor for HD patient survival and that it has a shorter lifetime in comparison with AVF. However, our results stem from a retrospective study, and an adequately powered prospective randomised controlled trial would be necessary to prove causality of the association of TDC with worse HD patient outcome.

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Contributors VP participated in designing the study, collected and analysed data and wrote the manuscript. BM, MG and KM participated in designing the study and collection of the data, and critically reviewed the manuscript. AL, BK and IŽ participated in designing the study, collected data and critically reviewed the manuscript. MK supervised the design of the study, coordinated and supervised data collection and analysis, and participated in writing the manuscript.

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Table 4 Causes of AVF function cessation

| Cause                          | N (%) |
|--------------------------------|-------|
| Death of a patient             | 5 (38.5) |
| AVF thrombosis                 | 4 (30.8) |
| Vein rupture                   | 2 (15.4) |
| Difficult AVF puncture or inadequate blood flow | 2 (15.4) |

AVF, arteriovenous fistula.

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