**Factors affecting long term survival of tunnelled haemodialysis catheters: a prospective audit of 812 tunnelled catheters**

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## Introduction

Haemodialysis requires repeated, secure access to the bloodstream whilst ensuring an adequate rate of blood flow. The arterio-venous fistula (AVF) represents the optimal means of providing such access, but arterio-venous grafts (AVGs) and cuffed tunnelled central venous catheters (TVCs) may be required where formation or maturation of a fistula is awaited, AVF formation is not possible for medical or personal reasons, or other routes of access have failed. Particularly in the latter group of patients, TVCs are relied upon to provide a means of permanent vascular access, and they do have a number of advantages in this respect. TVC placement is straightforward and can be performed by nephrologists, radiologists or surgeons, they can be used immediately once inserted, connection to the dialysis circuit is straightforward and needle free, and catheters provide sufficient blood flow to allow adequate haemodialysis (1-3). They do, however, suffer from a number of disadvantages, particularly catheter-related bacteraemia and sepsis (4), blockage and dysfunction (either by thrombus or fibrin sheath) (5;6), malposition and/or migration (7), an increased risk of central venous stenosis (8;9) and eventual device failure. There is also an association between TVCs and an increased risk of mortality, when compared to AVFs (10). Despite these problems, a combination of under-provision of vascular access surgery in the UK, late referral and co-morbidity means that a considerable number of our patients still utilise TVCs in the medium- to long-term - 27.5% from the most recent UK Registry data, and will continue to do so for the foreseeable future.

Since their first description by Schwab et al in 1988, a number of differing designs of TVC have evolved to try and minimise some of the problems associated with their use. Separation of the two intravascular tips of the device (“split-tip”) is reported to reduce fibrin sheath formation, catheter thrombosis and hence late malfunction – as well as recirculation (11;12), the design of the lumens and pattern of holes at the end of the catheter has been modified to improve blood flow and reduce recirculation, and catheters are now available in a variety of pre-curved lengths to aid placement and avoid kinking. Although the development of TVCs has revolutionised the management of patients requiring renal replacement therapy, their frequent complications present nephrologists with a classical 'double edged sword'- as one review recently put it, we 'hate living with them, but can't live without them' (13). Given this technological Faustian pact, use of TVCs should be informed and guided by knowledge of their complications, and an insight into their longevity and limitations. When it comes to TVCs, 'there are many questions, but few answers' (14)

In this study we present the results from an audit of all tunnelled catheter insertions performed at our institution over a 6 year period. We have evaluated the outcomes and complications of 4 different catheters:

a) Split-Cath ® III™ (Medcomp®) – dual lumen catheter with end and side ports
b) HemoSplit™ (Bard Access Systems) – pre-curved dual lumen catheter with end and side ports
c) Tesio twin catheter (Medcomp) – two entirely separate catheters, with end and side ports
d) Permcath™ (Quinton Instruments) – dual lumen catheter with end ports only

In addition to the type of TVC used, we have assessed whether site of insertion (right or left internal jugular vein or femoral vein) may have implications for longevity, and whether the performance of a patient's first TVC may be different to that of subsequent lines.

## Subjects and Methods

Setting – Lister Dialysis Programme

The Lister Renal Unit comprises three dialysis units providing renal replacement therapy to a population of approximately 1.2 million people. Throughout the period of study the units were treating between 300 and 400 haemodialysis patients.

Our patients use high-flux biocompatible membranes (predominantly polysulphone). Microbiological water purity is checked monthly to ensure compliance with tight chemical and microbiological standards (<0.1 cfu/mL and <0.03 EU/mL). Bicarbonate was used exclusively as buffer. On-line post-dilution haemodiafiltration (HDF) is the preferred modality for patients with minimal residual renal function (KRU < 1 ml/min)

and above average body weight. Between 60 and 70% of patients dialysed through an arterio-venous fistula with the majority of the remainder using tunnelled lines.
Dialysis prescription is individualised using a 2-pool kinetic model to ensure a total Kt/V (residual renal function + dialysis) of 1.2 per session for thrice-weekly dialysis, as described previously.

Data Collection:

Data of 812 TVCs undertaken in 492 patients was prospectively collected. The catheters were inserted between 13/1/00 to 28/12/05 (6 years) with minimum follow up of 1 year. 181 Split-Cath catheters were inserted, 395 Tesio catheters, 109 Permcaths and 127 Hemosplit catheters. 314 TVCs were inserted in women (39%) and 498 in men (61%); average age was 62.6. 211 patients were diabetic (26%). In total the study comprised 212,048 patient catheter days (7068 patient catheter months).
In 380 cases the tunnelled dialysis catheter was the first TVC the patient had received and in 432 cases the patient had received one or more previous TVCs.
TVCs were placed in the right internal jugular vein on 516 occasions, the left internal jugular in 165 occasions, the femoral veins (right or left) in 120 occasions and the subclavian veins (right or left) in 11 cases.
In 358 cases the TVCs were inserted in an operating theatre setting, by a surgeon, almost exclusively using fluoroscopic guidance. Of the 454 non-surgical cases the vast majority of TVCs were inserted in a dedicated procedures room on the acute nephrology ward, with monitoring (blood pressure, pulse oximetry and electrocardiography) but no fluoroscopic guidance. In the remaining cases (n=34) the catheters were inserted under fluoroscopic guidance by a physician in the radiology angiographic suite.
Choice of TVC design reflected the preference of the operator, the availability on the ward or in theatre, and in a few patients there were considerations of size. Ward lines were predominantly inserted by 3 physicians (AF, JS and PW), and theatre lines by 4 surgeons (including SS and HHT).

Statistics

Kaplan-Meier survival plots (curve generated as a staircase line with symbols at censored observations) were obtained using the program GraphPad Prism® 4, and curves compared using the logrank test. The relative importance of parameters, found to have a significant effect on line survival by this method, was determined by Cox Regression Analysis (SPSS).

## **Results**

Indications for insertion

In 150 (18%) cases TVCs were inserted in patients presenting with acute renal failure. In 133 (16%) patients were classified as having chronic renal failure; these patients had been followed up for a minimum of 3 months. 119 (15%) patients had catheter insertions following withdrawal from peritoneal dialysis, and 119 (15%) after failed (predominantly clotted) a-v fistulas. The commonest indication for TVC insertion was re-insertion after previously placed catheters had failed and been removed (n= 291, 36%).

Reasons for failure of line

In 17 cases (5%) TVCs were unable to be inserted for technical reasons, in 22 cases (6%) the TVCs never functioned because of mal-position or kinking of the catheter (counted as an immediate failure). 147 TVCs (43%) were removed after they became irreversibly blocked, and 111 (32%) after infection. 40 lines (12%) were accidentally pulled out or fell out. 5 (1%) were removed after developing a hole in one of the catheters.

The remaining 470 TVCs were censored, for the following reasons:

- TVC removed - no longer required – functioning a-v fistula – 174 (37%)
- TVC removed - no longer required – functioning Tenckhoff catheter – 26 (6%)
- TVC removed - no longer required – functioning renal transplant – 28 (6%)
- TVC removed - no longer required – recovered native renal function – 15 (3%)
- Patient died with functioning TVC – 170 (36%)
- TVC still working at time of completion of audit (31/12/2006) – 44 (9%)
- Patient lost to follow up (moved out of area) – 13 (3%)

Survival

Median survival of all TVCs is 506 days (approx 17 months).

There is a significant difference in survival between the first and any subsequent TVC insertion (median survivals 647 and 403 days respectively, approx. 22 and 13 months).

Operator does not appear to affect overall TVC survival. Equally neither age nor sex of patient demonstrated a significant effect on TVC survival. Diabetic status however did have a significant negative influence on survival (p= 0.0113).

The influence of insertion site on all TVCs: The internal jugular route is most favourable, and significantly better than left internal jugular route, which in turn is significantly better than the femoral route (median survivals of 633, 430 and 116 days respectively).

Although this is not a randomised study, we explored the influence of catheter design on survival. Initial analysis shows that overall the Hemosplit and Tesio catheters survived significantly longer than the Permcath and Split-Cath, but when we removed the influence of insertion site, by comparing just right internal jugular catheter survival, there was no significant difference between the Hemosplit, Tesio and Split-Cath, but all three survived longer than the Permcath (p=0.003). This difference was not apparent when a sub-analysis of only the first right internal jugular catheters was undertaken but reappeared on the sub-analysis of second and subsequent catheters, and a separate analysis of left internal jugular lines.

An analysis of all femoral lines (n=120), showed a significant survival benefit of Tesio catheters over Split-Caths and Permcaths.

Cox Regression Analysis (Backwards LR) (SPSS)

In a Cox proportional hazards model, the design of TVC, its position, whether it was the first or a subsequent catheter, and whether or not the patient was diabetic, were all significant independent predictors of line survival.

Hemosplit catheters (by 41%) and Tesio catheters (by 33%) were less likely to fail, and Permcaths 57% was more likely to fail than Split-Caths.

TVCs in the left internal jugular vein (by 54%), femoral vein (by almost 3 times more) and in the subclavian vein (by approximately 2 times more) were all more likely to fail than lines in the right internal jugular vein.

## Discussion

Patients on haemodialysis via tunnelled central venous catheters (TVCs) for 3 years demonstrate a 47% increased mortality compared with matched controls using AV fistulas (15). Indeed central venous access is considered to be the most important risk factor for infection and death in patients receiving renal replacement therapy (16). TVCs significantly increase the risk of vascular stenosis and occlusion, and compromise maturation and patency of subsequent arterio-venous fistulas and grafts (17). It is entirely appropriate therefore that the Dialysis Outcomes Quality Initiative put forth by the US National Kidney foundation (NKF) has recommended that less than 10% of all chronic maintenance haemodialysis patients should use dialysis catheters for more than 3 months in the absence of a maturing definitive vascular access (18).

There is disappointing progress towards this target. In the US 23% of haemodialysis patients were dialysing through catheters (a review published in 2002) (19) and in the UK in 2005 there were 29% of prevalent patients using catheters (20).

As a result of shortages of surgical theatre lists, the prevalence of catheters in our units in recent years has varied between 30 and 40%. This results in a steady stream of failed catheters requiring replacement; which was the commonest indication of catheter insertion (36%). A further 16% of TVC patients had been followed up for a minimum of 3 months. Some of these patients had undergone a-v fistula surgery but the fistula had failed or had not sufficiently matured for use, others had changed preference of dialysis modality with insufficient time to fashion an a-v fistula, and in a few, lack of definitive access surgery reflected failings in timely referral to, or delays in, surgery. 18% of TVC patients presented sufficiently late to preclude fistula creation.

The commonest cause for catheter failure necessitating removal was irreversible blockage (43%), predominantly thrombosis and fibrin sheath formation. Infection resulted in removal of 32% of catheters. A surprisingly high proportion of TVCs (12%), were accidentally pulled out or fell out. We believe repeated traction, either by accidental snagging of the catheter when changing clothes, or by injudiciously placed dialysis lines, were responsible.

Modern tunnelled dialysis catheters demonstrate reasonable survival, albeit often inferior to native arterio-venous fistulas. Duncan et al, in an impressive study of 623 Tesio-Caths inserted in 435 patients, demonstrated a censored functional catheter survival of 77.8% at one year and 44% at 3 years (3). Wang et al followed up 303 first Tesio catheters in 200 patients, demonstrating a catheter survival of 60% at one year, and 51.5% at 3 years (21). By contrast, Cetinkaya et al, studying 92 Ash-Split catheters in 85 patients, demonstrated a median survival of only 289 days (22). In addition some outstanding survival figures have been reported. Di Iorio et al, studying a mix of 98 dialysis catheters (predominantly Vas Cath Soft Cell catheters, Bard), has reported an 82% catheter survival at 84 months (23). Tesio et al, following up 108 Tesio catheters inserted in the early 1990s reported a 93% one year, 82% five year, and 32 % seven year catheter survival (24). In our study, the median survival all lines was 506 days (1year survival 61%, 3 year survival 22%). The very first tunnelled catheters, inserted into TVC naïve patients, demonstrate the best longevity (median survival of 647 vs 403 days, first vs subsequent lines). Subsequent TVCs were 39% more likely to fail on Cox proportional hazards modeling.

There is now little doubt that ultrasound guided insertion of central venous catheters improves insertion success rate and reduces complications. Resource limitations in the UK preclude the widespread use of fluoroscopic guidance. Our data fail to show a benefit in terms of catheter survival from fluoroscopic insertion by surgeons in an operating theatre, over ‘blind’ insertion by physicians in a dedicated ward based procedures room. However we would certainly not suggest that fluoroscopic assistance is unnecessary, indeed experience has taught us that it is particularly important in more ‘complicated’ catheter insertions, for example left sided catheters in patients with a history of previous catheter insertions.

Patient sex does not appear to be a significant factor in catheter survival. Some have suggested that in the elderly, TVCs are the vascular access option of choice, and our data certainly do not demonstrate a significant influence of age on catheter survival. But again, we would not suggest discriminating against the elderly by condemning them to TVCs unless there are specific contraindications to arterio-venous fistulas.

A history of diabetes mellitus does significantly adversely affect catheter survival ($p=0.0113$). Diabetics were 44% more likely to fail on Cox proportional hazards modeling.

The optimal site for placement of TVCs is the right internal jugular vein. Not only is the anatomy favourable, with a relatively straight route from internal jugular, to the right brachio-cephalic (innominate) vein, and thence to the superior vena cava, but the length, typically 15 or 16cm (as opposed to 20-23 cm for the left internal jugular) is shorter, and hence the ‘dead space’ within the catheter is reduced, and presumably less liable to clot. This is borne out by our data. Right internal jugular catheters survive significantly longer than left internal jugular catheters, which in turn survive longer than femoral catheters (median survival 633, 430 and 116 days respectively). That tunnelled femoral catheters perform poorly will surprise few clinicians who have had experience of their use, but our data show 50% have failed by 4 months, and over 80% have failed by a year, starkly illustrating their limitations as a reliable vascular access. Indeed these survival figures are an improvement on the 59 day median survival of femoral TVCs reported by Maya and Allon (25). Repeated bending of the catheter body and propensity of the exit site to become colonised with bacteria, a consequence of their anatomical site, presumably predispose to thrombosis and infection. On Cox proportional hazards modeling, TVC position proved to be the most influential factor determining survival.

There has been a paucity of data regarding survival of different catheter designs. Richard et al, in a randomized prospective evaluation, compared the performance of 36 Tesio, 38 Ash Split (similar to Split-Cath) and 39 Opti-flow catheters, but given the relatively small numbers, were unable to demonstrate a significant difference in survival (26). Trerotola et al, comparing 132 Ash-Split and Opti-flow catheters, were able to demonstrate a significant survival advantage for the Ash-Split (p= 0.02) (12).

We compared the performance of 4 types of commercially available tunnelled catheter. Two catheter designs – the HemoSplit and the Tesio twin catheter performed significantly better than the Split-Cath III and Permcath (median survival 727, 608, 308 and 286 days respectively. There was no significant difference between the Hemosplit and Tesio survival). Using Cox Proportional Hazard modelling, the design of the TVC was confirmed as an independent predictor of line survival, and the Hemosplit and Tesio designs again demonstrated best survival.

In patients with their first right internal jugular catheter, the differences in survival disappear, all catheters performing relatively well. The differences in performance become apparent again when assessing survival of second and subsequent right internal jugular catheters. In this subgroup, all catheters significantly outperformed the Permcath; the Hemosplit seemingly surviving the best, although this didn't reach statistical significance. Similar findings were observed in patients with left internal jugular catheters. In the femoral site, the Tesio catheter performed best, significantly better than the Permcath and Split-Cath (but not reaching significance above the Hemosplit). Perhaps it was the lack of side ports, or of separation of the end catheters, that contributed to the general poor performance of the Permcath.

We did not study factors influencing infection rates in our study, which has been covered in several other studies. We also appreciate that a limitation of the study was that it was not randomised.

The economics of haemodialysis access are staggering. The cost in the US alone of maintaining vascular access was over 1 billion dollars in 2001 (27). Given the current difficulties in vascular access provision, there is likely to be a long lasting reliance on tunnelled dialysis catheters. Clinicians will need accurate data regarding catheter survival, mode of insertion and design. Further randomised controlled studies are required to inform clinical practice in vascular access; an area which is likely to be of increasing consequence in the future.

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