Cost-effectiveness of three strategies of managing tunnelled, cuffed haemodialysis catheters in clinically mild or asymptomatic bacteraemias

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Abstract
Background. Immediate tunnelled, cuffed catheter (TCC) removal is the current standard of care when bacteraemia is associated with severe clinical symptoms. When minimal or no symptoms are present, the optimal strategy of TCC management is controversial. The following three strategies have been proposed: TCC 'salvage' (antibiotic administration without TCC removal), TCC exchange over a guidewire with antibiotics or immediate TCC removal with delayed reinsertion and antibiotics.

Methods. We developed a decision–analytic model to assess the cost-effectiveness of each strategy for episodes of TCC-associated bacteraemia presenting with minimal symptoms, in a hypothetical cohort of haemodialysis patients followed for a 3 month period. Data regarding the probability of treatment failure due to recurrent infection for each strategy, secondary infectious complications and patient mortality were obtained from existing clinical trials and from the 1998 United States Renal Data System database. Costs were substituted with the current 2000 New York hospital charges.

Results. Tunnelled, cuffed catheter exchange over a guidewire was associated with a reduction in net charges of $5241 and $750 when compared with TCC salvage and immediate TCC removal, respectively. The expected 3 month patient survival for TCC guidewire exchange and immediate TCC removal were similar (93%), whereas survival for TCC salvage was worse (89%). Tunnelled, cuffed catheter guidewire exchange remained the most cost-effective strategy when the probability of treatment failure with recurrent bacteraemia in 3 months was <25% for this strategy.

Conclusions. Tunnelled, cuffed catheter guidewire exchange is the most cost-effective strategy of catheter management when mild or no symptoms are present.

Keywords: bacteraemia; catheter management; haemodialysis; cuffed catheters

Introduction
Tunnelled, cuffed central vein catheters (TCC) are an important means of delivering haemodialysis to patients who require immediate initiation of dialysis but are without a mature, functioning arteriovenous fistula or graft, and in patients in whom a more desirable vascular access is not feasible [1,2]. Bacteraemia associated with TCC is a major complication and the incidence is an average of 3.13 episodes per 1000 catheter days [3–8]. Serious metastatic infections occur in ~30% (range: 13–44%) of episodes of TCC-associated bacteraemia. These include osteomyelitis, septic arthritis, infective endocarditis, epidural abscess and death [5,6,9].

The appropriate strategy for catheter management in cases of TCC-associated bacteraemia is controversial. Immediate TCC removal with delayed insertion is recommended when TCC-bacteraemia is associated with severe symptoms, such as clinical signs of sepsis, TCC-tunnell tract involvement or persistent fever (>72 h duration) [5,6,9–11]. However, in patients with minimal or no symptoms, who remain afebrile after 72 h of antibiotic therapy, three strategies have been proposed for catheter management of TCC-associated bacteraemia. These include TCC ‘salvage’, in which antibiotics are administered without catheter removal, exchange of the TCC over a guidewire for a new TCC within 3 days of bacteraemia or immediate TCC removal with delayed reinsertion when blood cultures are negative [5,10–16]. In fact, clinicians may be more likely to attempt TCC salvage in cases of asymptomatic bacteraemia, when the TCC exit and tunnell site appear clean.
The advantage of the salvage approach is the preservation of haemodialysis vascular access, uninterrupted haemodialysis, low immediate costs and both patient and physician convenience. However, TCC salvage has been associated with a high treatment failure rate (~66%) [5,6]. The guidewire exchange approach also has the advantage of vascular access preservation, uninterrupted haemodialysis scheduling and, most importantly, relatively low treatment failure rates (~18%), comparable to that reported for immediate TCC removal [10,12–14]. The major disadvantage of this approach is the necessity of an invasive procedure, which is a cause of patient inconvenience and higher immediate cost. Tunneled, cuffed catheter removal with delayed reinsertion is the most conservative approach. Data regarding treatment failure rates in cases of ‘mild’ TCC bacteraemia using immediate TCC removal are absent in the existing literature, as this strategy is usually reserved for severe symptomatic cases. One would predict treatment failure rates to be equal or lower than those associated with the guidewire exchange approach [10,12–14,16]. The disadvantage of TCC removal is the potential for loss of vascular access, added immediate costs and a high degree of patient and physician inconvenience due to the need for multiple procedures, including temporary femoral vein cannulation.

No prospective randomized studies exist which compare these strategies for catheter management in episodes of ‘mild’ TCC-bacteraemia in haemodialysis patients. The purpose of our study was to use a decision–analytical model to evaluate the clinical and economic outcomes associated with each of these strategies, from the perspective of the physician and the health-care payer.

Subjects and methods

Decision tree and underlying assumptions of the model

A decision model was created to evaluate and compare the outcomes associated with three management strategies of TCC-bacteraemia.

The hypothetical patient cohort for this model consisted of chronic haemodialysis patients dialyzing using a TCC for long-term vascular access (minimum 3 months) and who were at risk for TCC-associated bacteraemia. A bacteraemia was considered to be TCC-related when positive blood cultures were obtained from the TCC in the presence of an exit site infection or when other primary sources of bacteraemia were absent [5,10]. Only TCC-bacteraemias in which there was an absence of severe symptoms, such as clinical evidence of sepsis and/or a TCC-tunnell tract infection, and who became afebrile after 72 h of antibiotic therapy, were included in the cohort. The time period of analysis was from the onset of TCC-bacteraemia and for 3 months of follow-up. This 3 month period was chosen because it is a clinically relevant period of time for the evaluation of bacteraemia recurrence and for the development of secondary metastatic infectious complications. In addition, in all prior studies evaluating TCC-bacteraemia, the mean duration of follow-up was between 45 and 90 days [5,10–12].

In the decision model, one of three strategies of managing a TCC-bacteraemia could be used: (i) TCC ‘salvage’, in which the TCC remains in place during antibiotic therapy; (ii) exchange TCC over a guidewire for a new TCC within 3 days (without waiting for negative blood cultures); or (iii) immediate removal of the TCC with delayed reinsertion after a minimum of 1 week after blood cultures turned negative (Figure 1). We based our model on all available published series on TCC-bacteraemia [5,6,10–16].

The decision tree depicts six chance occurrences following TCC-bacteraemia: (i) the chance that a procedural complication occurs during TCC guidewire exchange; (ii) associated with immediate TCC removal—initial TCC removal, three temporary femoral haemodialysis catheter insertions and new TCC implantation; (iii) the chance that a procedural complication is serious; (iv) the chance that there is no recurrence of bacteraemia with the same organism (treatment success) within 3 months for all three approaches; (v) the chance that a recurrent bacteraemia is associated with complications (i.e. septic arthritis, osteomyelitis, endocarditis or epidural abscess); and (vi) the chance that the patient will die during the 3 month period. We assigned the utilities using a simple binary utility scale in which survival was assigned a utility of 1 and death a utility of 0.

Probability of events and sensitivity analysis

Each of the chance occurrences described above are assigned a base-case value, which is determined by obtaining the mean prevalence of this occurrence reported in the literature. For example, the mean prevalence of recurrent bacteraemia in 3 months associated with the TCC salvage strategy is 66%. The determination of expected total costs, patient survival and the cost-effectiveness ratio will be determined for each TCC strategy by multiplying the probabilities (base-case value) for every chance occurrence associated with that strategy, or ‘rolling back’ the decision analysis tree. One value is provided for the cost, patient survival and cost–benefit ratio for each strategy. Inserting a range for each base-case value (mean probability) allows for a more detailed analysis. The range of probabilities for each chance occurrence can be determined from the literature or can be determined by the investigator performing a query. For example, one might be interested in determining which strategy is most cost-effective if the recurrence of bacteraemia associated with the TCC salvage approach is <66%. Ranges for the probability of a particular a chance occurrence are used when performing a sensitivity analysis and for determining a range of costs or survival probabilities. The base case and ranges of event probabilities for this analysis are listed in Table 1.

The only data utilized were from patients presenting with ‘mild or no symptoms’ and a clean TCC exit site and tunnell appearance, and in which 3 month follow-up data was available. In addition to the published data in the literature, we added our unpublished prospective series of 77 cases of TCC-bacteraemia. Of these, 38 met criteria as having ‘mild or no symptoms’, and 16 were managed using TCC salvage, 10 TCCs were changed over a guidewire and 12 TCCs were removed with delayed reinsertion. Three month follow-up data were available in 19 cases at the time of this study (seven TCC salvage, five TCC guidewire exchange and seven
immediate TCC removals). The base case and range for the probability of treatment failure due to recurrent bacteraemia (66%) and metastatic infectious complications following TCC salvage (30%) were based on two uncontrolled observational studies and from our series [5,6]. For the sensitivity analysis, we were interested in evaluating the difference in cost-effectiveness between treatment strategies over a range of probabilities of unsuccessful TCC-salvage (50–85% treatment failure) [5,6,11]. The base case and range of probabilities of treatment failure (18%) and infectious complications (3%) following guidewire exchange were obtained from three observational series and our data [6,10,12]. For the sensitivity analysis, we varied the probability of treatment failure associated with guidewire exchange, again due to variability
of reported 3 month treatment failure rates among all series using this strategy (10–50%). Due to the absence of data from the existing literature on the outcome of immediate catheter removal in ‘mild’ TCC-bacteraemia, we estimated the probabilities of treatment failure (15%) and secondary infectious complications (2%) using data from our series and using the assumption that predictable outcomes would be comparable or lower than those reported with guidewire exchange. In addition, a sensitivity analysis over a range of probabilities for treatment failure (10–50%) was performed [16].

The likelihood of developing a procedural complication, including three femoral vein cannulations and a new TCC insertion into internal jugular vein, and the probability of that complication being of a serious nature, were obtained from two sources. The first is a study by Raja et al. [17] reporting on the prevalence of complications in 121 femoral vein haemodialysis catheter insertions (10% prevalence for each femoral catheter procedure: 9% mild, 1% severe). The prevalence of complications associated with TCC insertion was obtained from a prospective study of 190 TCC insertions (10% per TCC insertion: 9% mild, 1% severe) [18]. We did not find any reported complications associated with catheter exchange over guidewire in the five studies evaluating this procedure (in a combined total of 175 tunnelled, cuffed haemodialysis catheters) [10,12–14,16]. A combined review of five publications reporting on complications of 1386 guidewired exchange procedures in non-tunnelled venous catheters yielded only eight complications (one pulmonary embolism, seven haemothoraxes) [19–23]. The combined estimated complication rate associated with the guidewire exchange procedure is ~0.5%. One of the assumptions of this analysis was that the procedural complication rate for this technique was 0.5%. The 3 month mortality probability was estimated using data from the 1998 US Renal Data System report [24]. The mean age of haemodialysis patients dialyzing with a TCC is 56 years and 40–50% are diabetic [9,10]. Septicaemia is associated with a 2.4-fold higher all-cause mortality in haemodialysis patients [25]. These data were used to derive an estimated probability of death in 3 months after a successfully treated episode of TCC-bacteraemia [(3%, 3 month mortality rate) × 2.4 ~ 6–7%] [24,25]. The 3 month mortality rate was adjusted according to treatment failure and the development of procedural or infectious complications.

**Costs**

Because of the difficulty determining costs, or actual resource utilization, charges (as represented by list prices) were used as a substitute for cost in this model. These charges reflect the 2000 prices at Montefiore Medical Center, Bronx, New York. Both base-case charges and a range for various procedures and outcomes are provided in Table 2.

### Table 1. Decision analysis probabilities

<table>
<thead>
<tr>
<th></th>
<th>Base-case value</th>
<th>Range used in sensitivity analysis</th>
<th>References</th>
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<tbody>
<tr>
<td>TCC salvage</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Recurrent bacteraemia at 3 months</td>
<td>66%</td>
<td>(50–85)</td>
<td>5,6,a</td>
</tr>
<tr>
<td>Complicated bacteraemia</td>
<td>30%</td>
<td>(13–44)</td>
<td>5,6,9</td>
</tr>
<tr>
<td>TCC change over guidewire</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent bacteraemia at 3 months</td>
<td>18%</td>
<td>(10–50)</td>
<td>6,10,11,a</td>
</tr>
<tr>
<td>Complicated bacteraemia</td>
<td>3%</td>
<td>(1–5)</td>
<td>6,10,11</td>
</tr>
<tr>
<td>Immediate TCC removal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent bacteraemia at 3 months</td>
<td>15%</td>
<td>(10–50)</td>
<td>14,a</td>
</tr>
<tr>
<td>Complicated bacteraemia</td>
<td>2%</td>
<td>(1–5)</td>
<td></td>
</tr>
<tr>
<td>Procedural complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporary femoral vein catheter</td>
<td>10%</td>
<td></td>
<td>22</td>
</tr>
<tr>
<td>TCC insertion into internal jugular vein</td>
<td>10%</td>
<td></td>
<td>23</td>
</tr>
<tr>
<td>Guidewire exchange</td>
<td>0.50%</td>
<td></td>
<td>17–21</td>
</tr>
<tr>
<td>Patient 3 month survival</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Uncomplicated TCC-bacteraemia</td>
<td>6%</td>
<td></td>
<td>24,25</td>
</tr>
<tr>
<td>Complicated TCC-bacteraemia</td>
<td>22%</td>
<td></td>
<td>24,25</td>
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*Unpublished data from Montefiore Medical Center, Hartford Hospital and East Hartford Dialysis Prospective Series.

### Table 2. Decision analysis costs

<table>
<thead>
<tr>
<th></th>
<th>Costs [$] for year 2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful TCC-salvage</td>
<td>772 (500–900)</td>
</tr>
<tr>
<td>Treatment failure with uncomplicated infection</td>
<td>1544 (872–4319)</td>
</tr>
<tr>
<td>Treatment failure with complicated infection</td>
<td>32 799 (26 149–56 590)</td>
</tr>
<tr>
<td>(septic arthritis, osteomyelitis, endocarditis, epidural abscess)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>17 531 (8075–35 422)</td>
</tr>
<tr>
<td>TCC guidewire exchange</td>
<td>4227 (4427–4627)</td>
</tr>
<tr>
<td>TCC removal</td>
<td>5127 (4527–5727)</td>
</tr>
<tr>
<td>Procedural complication, serious</td>
<td>32 799 (5000–56 590)</td>
</tr>
</tbody>
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The estimated base-case cost for treatment failure with uncomplicated infection was based on an additional 6 weeks of antibiotic administration. The high end within the range for this value also includes the cost of TCC removal, three temporary femoral vein catheters, TCC reinsertion and a chest radiograph. The base-case cost of treatment failure with complicated secondary infection is an estimate of the cost of endocarditis with septic arthritis: the cost of TCC removal, four temporary femoral vein catheters, 7 days of hospitalization on the medical floor, transesophageal echocardiogram, three sets of blood cultures, two chest radiographs, magnetic resonance imaging of a joint, consultant fees and 6 weeks of antibiotics. The low end within the range of this cost was estimated for a shorter period of hospitalization and the high range was estimated as the cost of an epidural abscess, requiring an MRI of the complete spine, surgery, several days in the surgical intensive care unit, as well as a prolonged hospital stay on the floor.

The base case for the cost of death was estimated based on a prolonged hospital stay on the medical floor and in the intensive care unit, and included the cost of prolonged antibiotics, imaging studies, laboratory testing and CPR. The wide range of this value was largely attributable to the number of hospital days (early vs late death relative to hospitalization). The cost of a mild procedural complication after temporary catheter femoral vein cannulation or TCC insertion was determined to be equivalent to the cost of an additional hospital stay for observation. The cost of a serious procedural complication was estimated to be the cost of surgical repair of a lacerated artery, several days of hospitalization in the surgical intensive care unit and hospital floor, in addition to imaging and laboratory costs. The range of this value was largely due to variability in the length of hospital stay.

Cost-effectiveness and sensitivity analysis

The outcomes that were analysed for each treatment strategy were the accrued cost (charges) and success of treatment strategy. A cost-effectiveness ratio (net costs divided by the net effects i.e. probability of successful treatment) was also performed [26]. This provides an analysis of the average cost per successful treatment for each management strategy and their respective cost.

Sensitivity analyses were performed to evaluate the effect of varying the probabilities and costs of individual variables to encompass the outcomes reported in the published literature. The variables of interest were the probability of treatment failure for each strategy.

Computer analysis

A decision analysis software program (Tree Age, Data 3.5) was used to create the decision trees, perform the calculations for the model and conduct the sensitivity analyses.

Results

Baseline analysis

The expected total costs, 3 month patient survivals and cost-effectiveness ratios for each TCC strategy are provided in Table 3. The guidewire exchange strategy was associated with a reduction in net charges of $5241 and $750 compared with TCC salvage and TCC removal, respectively. Tunnelled, cuffed catheter removal and guidewire exchange were similar with respect to effectiveness (93% patient survival at 3 months) and both were superior to TCC salvage (89% patient survival at 3 months). In summary, TCC guidewire exchange was found to be the least expensive strategy and was associated with a high patient survival, whereas TCC salvage was the most costly strategy and was associated with the lowest patient survival.

Sensitivity analysis

A two-way sensitivity analysis of cost was performed in which a range of probabilities was provided for the following chance occurrences: treatment failure due to recurrent bacteraemia associated with TCC removal and treatment failure due to recurrent bacteraemia associated with guidewire exchange (Figure 2). These data show that TCC guidewire exchange was associated with lower total costs when the chance of recurrent bacteraemia associated with this strategy was <25%.

A one-way sensitivity analysis was performed to determine the variation in total costs accrued with TCC salvage over a range of probabilities of recurrence of bacteraemia at 3 months (50–85%) associated with this strategy (Figure 3). For the purpose of this analysis, the probability of recurrent bacteraemia at 3 months for the other strategies was kept constant (base-case values). The additional cost associated with the salvage approach, in comparison with the guidewire exchange strategy, ranged from ~$3000 to ~$8000 depending upon the probability of recurrent bacteraemia at 3 months (50–85%, respectively).

Discussion

We used decision-analytic techniques to evaluate the clinical and economic impact of using three different catheter management strategies in a hypothetical cohort of haemodialysis patients with ‘mild’ TCC bacteraemias. In an unpublished prospective series of 77 episodes of TCC-bacteraemia at Montefiore Medical Center and Hartford Hospital, 48% of patients met criteria for ‘mild’ TCC bacteraemia (TCC exit/tunnel tract without erythema or exudate and who became
afebrile after 72 h of antibiotic therapy). Our analysis indicates that TCC guidewire exchange results in reduced costs and improved or equivalent patient survival compared with the alternative strategies (TCC salvage and immediate TCC removal, respectively). In fact, the utilities do not take into account additional hospitalizations and suffering (due to repeated femoral catheterizations) that may be associated with
immediate TCC removal with delayed reinsertion. This model, therefore, potentially underestimates the superiority of the guidewire exchange strategy as compared with immediate TCC removal. Although the initial costs of changing over the wire are higher than those of salvage, the higher probability of treatment failure, infectious complications and patient mortality associated with the salvage approach presumably leads to an increase in the consumption of costly goods and services.

Limitations of the study

The assessment of costs was based on list prices available for our hospital (Montefiore Medical Center, Bronx, NY, USA) and these charges were used as a substitute for cost. These values do not represent true costs, as there is a wide variation in resource utilization based on individual case. Although sensitivity analysis partially addressed this problem it is not an accurate assessment and substitute for actual costs. The present cost analysis is limited to the present cost and health care environment in the US.

The clinical data (i.e. probabilities of events) were based on the findings reported in the literature from different studies and population groups. The criteria for entry of patients in these studies were not uniform. There is also a significant paucity of available data regarding the probabilities of various events occurring when different strategies are used, particularly for the outcome associated with TCC removal in mild bacteraemia. We addressed this by utilizing data from our own series of mild TCC bacteraemia. There were limited data available for the long-term outcome of these patients; therefore, the outcome point was limited to 3 months. We only considered two ultimate outcomes, survival and death. Although the clinical data were from multiple institutions, the costs were based on the prices from one hospital and thus the generalizability of costs for institutions in other geographical areas may differ. This was addressed by use of a broad range of costs while performing sensitivity analysis for the cost of complications.

The probability of treatment failure using the TCC salvage approach was obtained from the two existing reports evaluating this technique in TCCs used for haemodialysis. We did not include reports in which the antibiotic lock technique was utilized, which may be associated with improved outcomes. However, Figure 3 demonstrates the marginal costs (excess cost of salvage vs the other two strategies) for a range of possible outcomes for TCC salvage (50–85%). We performed a one-way sensitivity analysis (data not shown) for a broader range of theoretical outcomes associated with TCC salvage (0–85%) to determine the hypothetical threshold value at which TCC salvage would become the most cost-effective strategy. When the treatment failure rate associated with TCC salvage was 30% or less, TCC salvage became the most cost-effective strategy. Based on this analysis, it is theoretically possible that TCC salvage with antibiotic lock would be the preferred strategy of managing catheters if the recurrent bacteraemia rate in 3 months was 30% or lower. A randomized controlled trial is required to further evaluate and validate this model.

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References


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