Predicting Frailty and Catheter Infection

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Kidney failure refers to when kidneys loose the functionality to clean your blood and remove excess fluid from your body. Dialysis is a treatment procedure in which blood exits your body through vascular access to an external filter, where it is cleaned before re-entering the body. One procedure for dialysis includes using a venous catheter. Vascular access is the site in which blood is removed and returned during dialysis via a catheter. A catheter is a tube inserted into a vein, for example in your neck, (however other sites are used as well). The catheter has two chambers, allowing for a two-way flow of blood. According to the NIH (2010), catheters are not always ideal as they can become infected. Infections typically require medication and removal of the catheter and replacement.

Typically catheters can become infected due to not following proper care directions. According to the National Kidney Foundation (2010), keeping a catheter clean and dry, as well as wearing facemasks when opening the catheter to reduce bacteria from entering are important procedures to follow. It is imperative to be aware of signs of infection, including fever, chills, drainage, and redness around the catheter site.

The epidemiology of kidney failure is typically due to a variety of disease or immune problem. Kidney problems can be due to malfunction of the kidney, or due to other diseases which impact functioning of the kidney or due to genetic reasons. Glomerulonephritis is due to damage of the kidney. Acute nephritis refers to disorders which cause swelling of the structures of the kidney, usually caused from other disease symptoms. Polycystic kidney disease is inherited and refers to when cysts grow in the kidneys. Often, these issues with the kidneys lead to kidney failure and end-stage renal failure. Other complications however can lead to death, including infection.
Previous literature has examined predictors or risk factors of catheter infection. In study by Tovbin et al. (2001), elderly patients were examined with regards to several potential risk factors for catheter infection, including demographic data such as age and gender, as well as factors such as length of end-stage renal failure, diet and social support. Results indicated older age, gender (female), inadequate nutrition and lack of social support was related to severe catheter infection. A limitation of this study was that the data was collected retrospectively, thus information may not have been as accurate as if it were prospectively collected, the small sample size and the fact the sample was 66% female.

Age was a significant predictor of bacteria related infection in a study of 59 children who use catheters by Onder et al. (2006). Also, the comorbidity of HIV was a significant predictor. Regarding age, specifically children less than 10 years were associated with more rates of infection. It should be noted however, children also had different types of catheters in this study.

In a more recent study by Harwood et al. (2008), researchers examined characteristics associated with infections in tunneled catheters. Both data regarding care behaviors and characteristics of the sample were collected. Results indicated none of the characteristics were significant, while behaviors such as type of dressing and cleaning behavior were significant predictors. While some younger participants were included in this sample (minimum age = 18), the mean age was 62 years of age. This sample also had been receiving chronic hemodialysis treatment for an average of 3 years, which may point toward the weakness of the patients, however this aspect was not considered in the Harwood et al. study as a predictor.

The purpose of the present study is to investigate associations between variables in the data-set and the created variable, frailty. Also, characteristics such as gender and age as well as factors related to illness such as disease type and frailty will be investigated as covariates to
length of time before infection. The analyses in this study will attempt to flush out findings in
the literature. 1. Do males and females differ in regards to frailty or infection? 2. Is age related
to frailty or infection? 3. Does frailty or infection differ based on disease type? 4. Are frailty and
length of time before infection related? This study is largely exploratory in nature, and multiple
regression as well as survival analysis will be used to explore these relationships.

Method

Participants

It is unclear whether the participants were self-selected for the study or recruited. A total
of 38 individuals (74% female) ranging in ages from 10 to 69 years of age ($M=43$, $SD=15$)
participated in this study. Because of the difference in sex for the sample, caution should be
noted when reviewing results as the sample is heavily biased female. The results may only
generalize to females if a variable is found to be related to the response variable, thus multiple
regression is recommended to control for gender. No indication of race/ethnicity was provided
for the sample and we are not aware if the sample is restricted by geographic location, nor were
any specific inclusion/exclusion criteria provided.

Measures

Data collected included demographic information such as age, and sex. Age was coded
in years, and sex was dummy coded (1=male, 2=female). Disease type was also indicated, GN =
Glomerulonephritis, AN= Acute Nephritis,  PKD = Polycistic Kidney Disease or Other (See
Figure 1). Disease was a treated categorically, and was dummy coded with GN as the referent
group. The process for data collection was not included therefore we are unaware of the
accuracy of the information. A frailty estimate was calculated using a Newton-Raphson iterative
approach was added to the data set.
One unique aspect of the data set is that two data points for recurrence of infection for each participant is included. This is because a catheter that is inserted may need to be removed due to the infection. After the catheter is removed, the infection is then cleared, and after a 10-week interval a new catheter is inserted. A paired sample t-test was ran to determine if there were mean differences in the number of days it takes until infection sets in and no significant differences were found ($t(36) = .329, p = .744$). Correlation between the two variables also revealed a non-significant relationship, ($r = .01, p = .97$). The two sets of data will be used as follows for cross-validation: 1 set to fit a model and the second set of data to check if similar results when the model is fit on the second set of data. No data were missing; however an outlier was removed from the data (case 21) due to extremely high recurrence time which created issues as a multivariate outlier.

A backward approach using multiple regression was used to examine prediction of frailty. With the first half of the data ($N = 37$), a full model was first estimated, including predictors age, sex, (log of) days until infection from catheter insertion, and type of disease (dummy coded). Diagnostics revealed assumptions were met for the multiple regression. The ANOVA for the full model was non-significant, $F(6,30) = 2.27, p = .06$, $R^2_{\text{Adj}} = .17$. Dropping the variable which would increase the $R^2_{\text{Adj}}$ was accomplished by dropping a dummy coded variable, however dropping one categorical variable dummy coded would not make sense. Therefore, all but the one dummy coding of disease type that was significant (disease type =PKD) were dropped from the model. The second model predicting frailty included age, sex, PKD and (log of) days. The model was significant, $F(4,32) = 3.36, p = .02093$, $R^2_{\text{Adj}} = .21$. Dropping sex (non-significant) from the model improved the model. The model was significant, $F(2,33) = 4.59, p = .008566$, $R^2_{\text{Adj}} = .23$. The model was re-estimated without age which was non-
significant. Although dropping age from the model did not largely improve the model $R^2_{\text{Adj}}$, ($F(2,34) = 6.527, p=.00399 ~ R^2_{\text{Adj}} = .23$), the goodness of fit did not increase significantly.

Considering parsimony when deciding on nested competing models, the model with the least number of variables which explain the same amount of variance is kept. Lastly, dropping either of the last two variables increases the $R^2_{\text{Adj}}$, thus the last model is retained ($Y = 1.7983 + .90 \text{PKD} - .17 \ln (\text{R1})$). Beta coefficients reveal those patients with Polycystic Kidney Disease are associated with higher frailty scores, and those with lower number of days until catheter infection are associated with higher frailty scores. Since the “days until infection” variable was logged transformed, the beta coefficient for this variable is interpreted as: a 1% increase in number of days until infection is associated with an average -.17/100 units decrease in frailty.

Multiple regression was used to examine the prediction of frailty using the second half of the data. A full model was first estimated, including age, sex, (log of) days until infection from catheter insertion and type of disease. Diagnostics revealed assumptions were met for the multiple regression. The ANOVA for the full model was non-significant, $F(6,30) = 2.10, p=.08287, R^2_{\text{Adj}} = .15$. Again here, dropping the variable which would increase the $R^2_{\text{Adj}}$ would have been by dropping a dummy coded variable, which would not be interpretable with just dropping one categorical variable. All but the one dummy coding of disease type that was significant (PKD) were dropped from the model. The second model predicting frailty included age, sex, PKD and (log of) days. The model was significant, $F(4,32) = 3.07, p=.03009, R^2_{\text{Adj}} = .19$. Dropping age (non-significant) from the model improved the model. The model was re-estimated without age which was non-significant. Dropping sex from the model did improve the model, $F(2,34) = 6.488, p=.004104 ~ R^2_{\text{Adj}} = .23$.)
Dropping either of the last two variables increases the $R^2_{\text{Adj}}$, thus the last model is retained ($Y = 1.91 + .83 \text{ PKD} - .21 \ln \text{R2}$). Results are similar to the model tested on the first set of data, patients with PKD are associated with higher frailty scores, and those with lower number of days until catheter infection are associated with higher frailty scores. Since the “days” variable was transformed, this is interpreted as a 1% increase in number of days until infection is associated with an average -.21/100 units decrease in frailty.

A Cox proportional hazard regression survival analysis was performed to assess the effects of covariates: age, sex, disease, and frailty on prediction of survival, or the length of time before infection set in. A conservative alpha was set at .001, due to many tests estimated. There were 6 censored observations due to either catheters removed for other reason than infection or censored due to not experiencing infection (the data did not indicate differences). Survival time was predicted by the set of covariates, $R^2 = .66$. The R-squared represents the association between survival and the covariates tested. Covariates which predicted survival time included: Risk = -2.94 (sex) + 1.58 (frailty). Negative values are associated with longer survival times, therefore females have longer time without infection than males. Positive values are associated with shorter survival times. This means the higher the frailty score the shorter the time until infection. Regarding the hazard rations, for every one unit change in frailty, the risk of infection is four times likely and for every one unit change in sex, the risk of infection decreases about 94%. See Figure 2.

The same analysis was completed with the data from the second time the catheter was replaced. A Cox regression survival analysis was performed to assess the effects of covariates: age, sex, disease, and frailty on prediction of survival, or the length of time before infection set
in. The alpha was set to be .001, due to many tests estimated. An outlier was removed from the data (case 21) due to extremely high recurrence time. There were 12 censored due to either catheters removed for other reason than infection or censored due to not experiencing infection. Survival time was predicted by the set of covariates, \( R^2 = .62 \). The R-squared represents the association between survival and the covariates tested. Covariates which predicted survival time this time only included: Risk = 2.57 (frailty), although sex was approaching significance (\( p = .002 \)). This means the higher the frailty score the shorter the time until infection. Regarding the hazard ratios, for every one unit change in frailty, the risk of infection is 13.06 times likely. See figure 3.

**Discussion and Conclusions**

Findings of these analyses do not necessarily support those found in previous literature. Age was not a significant predictor however it may be because the more “extreme” ages (very young or very old) were predictors in other studies. The study is limited in that it doesn’t explore possible reasons for associations, including care and behaviors which may be associated to sex and/or frailty. This may be the reason why personal characteristics were not found predictors in the study which included caring of catheter in the model. Thus, other aspects such as other health issues, personal hygiene, as well as SES, for example may be predictors to consider in the future. Identifying predictors are useful in creating intervention programs which target specific groups which may be more prone to catheter infection.

**References**


Figure 1. Breakdown of Sample by Disease Type
Figure 2. Survival Function at mean of covariates Recurrence 1
Figure 3. Survival Function at mean of covariates Recurrence 2