Paper 1650-2014

Risk factors and outcome of spinal epidural abscess from incident hemodialysis patients from the United States Renal Data System between 2005 and 2008

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ABSTRACT

Spinal epidural abscess (SEA) is a serious complication in hemodialysis (HD) patients, yet there is little medical literature that discusses it. This analysis identifies risk factors and co-morbidities associated with SEA, as well as risk factors for mortality following the diagnosis using SAS. All incident HD cases from the United States Renal Data System for calendar years 2005 to 2008 were queried for a diagnosis of SEA. Potential clinical covariates, survival and risk factors were recovered using ICD-9 diagnosis codes. Log-binomial regressions were performed using PROC GENMOD to assess the relative risks, and Cox regression models were run using PROC PHREG to estimate hazard ratios for mortality.

INTRODUCTION

Spinal epidural abscess (SEA) is considered to be a localized abscess between the skull or vertebral column and the underlying dura mater. It can be a serious complication for HD patients. The most common symptoms seen in SEA patients are neurological deficits, back pain, and paralysis. SEAs have been well described in the literature, but there is limited information in HD patients. A five-year study at Long College Hospital in Brooklyn, New York looked at SEAs in 36 HD patients and compared them to 85 SEA patients that were not on HD. The mortality rate was higher in SEA patients on HD (23% vs. 7%). This study is the largest literature review of SEA in patients on HD to date.

The current project largely expands the above study by conducting a comprehensive data extraction of 660 SEA patients on HD from the United States Renal Data System (USRDS) between 2005 and 2008. The USRDS is a comprehensive dataset containing baseline clinical data, and all ICD-9 and CPT codes submitted to Medicare, on every HD patient in the United States. This dataset serves as the source for information on this project.

METHODS

We conducted a retrospective cohort study to determine risk factors for SEA in HD patients. Data were limited to individuals with SEA who had their first end stage renal disease (ESRD) service date (i.e. incident ESRD) between 2005 and 2008. Individuals were followed from the date of their first ESRD service through the end of the follow-up period (December 31, 2008). Demographic data were combined with information contained on the Centers for Medicare and Medicaid Services (CMS) Medical Evidence Report (CMS-2728) and hospitalization Medicare claims. All statistical analyses have been performed using Base SAS® version 9.3 at a significance level of 0.05.

In order to select the appropriate cohort, the primary exposure of interest has been chosen to be HD patient's vascular access, retrieved from CMS-2728 data set. Three types of vascular access exist: arteriovenous fistulas (AVF), arteriovenous grafts (AVG), and tunneled dialysis catheters. The primary outcome variable is the diagnosis of SEA, denoted by the ICD-9 diagnostic code of 324.1.

Since the USRDS does not automatically show each patient's diagnosis according to ICD-9 codes, for each condition we need to recover the diagnosis condition from its ICD-9 code.

Here is an example of identifying SEA in ICD-9 diagnosis:

```
data usrds.sea_analysis;
if substr(hsdiag,1,4) = '3241' then SEA = 1;
```

Other outcome variables include sex, race, ethnicity, year of first ESRD service, and age at which the patient starts hemodialysis. Relevant comorbid conditions and their respective ICD-9 codes are then recovered using similar method.

Table 1. Sample ICD-9 code for comorbid condition

Diagnosis	ICD-9 code
Hepatitis C virus	070.41, 070.44, 070.51, 070.54, 070.7, V02.62

For cases where multiple ICD-9 codes exist to describe the same comorbid condition, here is an example for identifying ICD-9 diagnosis for patients with Hepatitis C:

```
data usrds.sea_analysis;
if substr(hsdiag,1,5) in ('07041','07044','07051','07054','V0262') or
substr(hsdiag,1,4) = '0707' then hepc=1;
```

Univariate descriptive statistics have been conducted on all variables of interest using PROC TTEST and PROC FREQ. Chi-square tests have been performed on potential covariates of interest stratified by SEA diagnosis using PROC FREQ. Bivariate generalized linear models have been used to determine if there was an association between a diagnosis of SEA and other factors of interest under PROC GENMOD. Multivariate generalized linear models were used to determine relative contributions of the risk factors of interest to a diagnosis of SEA. Relative risks (RR) were estimated using a log-binomial model. Survival curves were obtained using PROC LIFETEST to determine the difference in survival times between SEA and non-SEA patients. Cox regression models were used to determine the relative hazard of death associated with an SEA diagnosis compared to other known risk factors for death in ESRD patients. We used bivariate and multivariable models to assess these associations. Using backwards elimination of non-significant variables, a final model was obtained, and the hazards ratios (HR) and 95% confidence intervals (CI) are reported.

RESULTS

The median age of the USRDS cohort was 65 years. SEA was identified in 660 out of 355,084 (0.19%) patients. Vascular access type at the initiation of HD included AVF in 47,732 (13.4%), AVG in 14,179 (4.0%) and vascular catheters in 293,173 (82.6%) patients.

Table 2. Sample demographic information of 660 HD patients with SEA

Parameter	Level	SEA Cohort	non-SEA Cohort	P-value
Gender (N, %)	Male	384 (58%)	198,216 (56%)	0.2436
	Female	276 (42%)	156,208 (44%)	
Age at first ESRD service (Median, range)		62.5, 24-90	65, 18-100	0.0007

Sample code for obtaining demographic information for categorical variable sex:

```
proc freq data=usrds.sea_analysis;
table sea*sex/chisq; run;
```

Sample code for obtaining demographic information for continuous variable incidence age:

```
proc ttest data=usrds.sea_analysis;
class sea;
var inc_age; run;
```

Within the SEA population, 58% of the patients are identified as male, which does not differ significantly from the overall USRDS cohort (p=0.2436). The median age is 62.5 years, 2.5 years younger than the overall USRDS group (p=0.0007).

The following table showcases the difference between unadjusted and adjusted relative risks and their respective 95% confidence intervals. Such results were obtained by performing the adjusted log-binomial regression in PROC GENMOD. Notice that a relative risk of greater than one means that a patient with such condition is more likely to be diagnosed with SEA. A relative risk of less than one indicates that a patient with such condition is less likely to be diagnosed with SEA. However, the relative risk calculation is only statistically significant if its 95% confidence interval does not include one.

Table 3: Sample relative risks of co-morbidities in SEA HD patients

Parameter	Level	Unadjusted RR	95%RR CI		Adjusted RR	95% RR CI	
Initial Access Type	Catheter	1.9082	1.4298	2.5465	1.3181	0.9856	1.7629
	AVG	1.6159	0.9935	2.628	1.1689	0.717	1.9055
	AVF	Ref	-	-	Ref	-	-

Below is sample code for calculating the unadjusted relative risk of access type. Notice that the reference group is AVF, and we are interested in finding the relative risks of patients whose access types are catheter and graft (AVG).

```
proc genmod data=sea_analysis order=formatted desc;
class accesstype(ref="AVF");
```

```
model sea = accesstype/dist = binomial link=log;
estimate 'Catheter' accesstype -1 1 0 / exp;
estimate 'Graft' accesstype -1 0 1 / exp;
run;
```

Notice the slight difference in adjusted relative risk for access type when all other covariates are included in the calculation from unadjusted relative risks.

We are also interested in finding out whether there is a survival advantage for SEA HD patients.

To obtain the survival curve and median residual lifetime for SEA HD patients, the following codes are used.

```
proc lifetest data=usrds.sea_analysis method=lifetable plots=survival;
time surv_time*death(0);
strata sea;
run;
```

Figure 1. Survival curve for HD patients stratified by SEA diagnosis

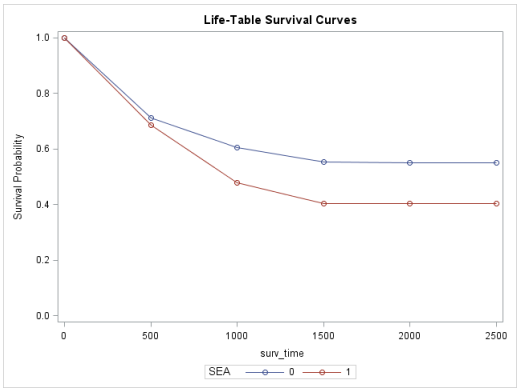

Figure 1 shows that more than half of the HD patients without SEA are still living at the end of study, whereas the median residual lifetime for SEA HD patients is roughly 2.5 years.

Table 4. Sample hazard ratios of co-morbidities regarding death in SEA HD patients

		Crude HR	95% HR CI		Adjusted HR	95% HR CI	
SEA		1.368	1.237	1.513	1.179	1.064	1.305
Age of Patient	≥ 65 years	2.541	2.513	2.569	2.254	2.228	2.28
	< 65 years	Ref	-	-	Ref		

Here is an example of obtaining crude hazard ratios for two age groups.

```
proc phreg data=usrds.sea_analysis;
class age65 (ref=first);
model surv_time*death(0) = age65 / rl ties = efron;
run;
```

When all significant crude hazard ratios have been included in the full model, we then used backward elimination to reduce the full model into a reduced model where all covariates are statistically significant. Notice the drop in hazard ratio for SEA. When calculating crude HR, SEA patients are 36.8% more likely to die than non-SEA patients. However, when adjusted for all other demographic characteristics and clinical characteristics, hazard ratio for SEA is no longer as big. The new adjusted hazard ratio means that SEA patients are 17.9% more likely to die than non-SEA patients.

CONCLUSION

SEA is an uncommon but serious complication of HD. Previously such condition has been difficult to study due to its rarity. We were able to conduct the largest cohort study to date and find risk factors and comorbidities of SEA on HD patients using various procedure steps in SAS® 9.3.

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