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POSTER ABSTRACTS

903.HEALTH SERVICES AND QUALITY IMPROVEMENT -MYELOID MALIGNANCIES

Time to Treatment for Patients with Suspected Acute Promyelocytic Leukemia (APL)

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Introduction:
Acute promyelocytic leukemia (APL) is a rare subtype of acute myeloid leukemia characterized by dysplastic promyelocytes which cause aberrations in coagulation, including hemorrhage and disseminated intravascular coagulation (DIC), leading to a rapidly fatal course if treatment is not initiated promptly. Early administration of all-trans retinoic acid (ATRA) in patients suspected of having APL is crucial for reducing morbidity and mortality. However, APL still exhibits a high early death rate in part due to failure to rapidly initiate ATRA. Therefore, we conducted a retrospective study to investigate the time it takes for ATRA to be ordered and administered to patients with suspected APL at our tertiary care University hospital. We also examined demographic and clinical variables to identify any opportunities for quality improvement.
Methods:
We queried our electronic medical record (EMR) for all adult patients without a prior diagnosis of APL from 2017-2021 who received at least one dose of ATRA at Thomas Jefferson University Hospital. Our analysis included 91 patients. We collected a wide range of demographic and clinical data (Table 1). The time of admission was defined as the time the admission order was placed in the EMR, and the time of administration was defined as the time the nurse marked the medication as administered. A simple general linear model was used to evaluate univariate association between each single covariate and each log transformed outcome. Model selection by Akaike information criterion (AIC) was conducted to identify the best model according to goodness of fit criteria. The smaller the AIC value, the better the model fit. The parsimonious models were obtained using backward elimination of non-significant predictors (p-values > 0.05) from the best models according to goodness of fit criteria (AIC).
Results:
The mean time for interval A (time from hospital admission to ordering ATRA) was 284 minutes, the mean time for interval B (time from ATRA order being placed to ATRA administration) was 104 minutes, and the mean time for interval C (time from admission to ATRA administration) was 388 minutes. Further analysis of the time intervals is presented in Table 2.
The results of the demographic and clinical variables (Table 1) show that the majority of patients were transferred from an outside hospital (89%) and admitted overnight (87%). Consequently, ATRA was most often ordered (76%) and administered (70%) overnight. Only 26 (29%) patients were ultimately confirmed to have APL. During the index admission, patients required a mean of 6 units of packed red blood cells and 9 units of platelets. A quarter of patients were noted to have signs or symptoms of bleeding upon admission.
The results of the multiple linear regression analysis are shown in Table 2. Only signs or symptoms of bleeding were associated with a statistically significant decrease in time to ATRA. Patients with signs of symptoms of bleeding experienced, on average, 39% less time from admission to ATRA being ordered (95% CI: 0.396-0.946, p=0.030) and 31% shorter time from admission to ATRA administration compared to those without signs or symptoms of bleeding (95% CI: 0.489-0.967, p=0.034).
Conclusions:
Our study highlights that, even at a large, resource-rich, academic medical center, the time to ATRA administration in patients with suspected APL is longer than optimal. The presence of bleeding was the only variable that significantly decreased the

time to ATRA. Earlier identification of bleeding risk (including evolving DIC or thrombocytopenia), increased recognition of possible acute leukemia, and more rapid hematology/oncology consultation could help to decrease the time to ATRA and to avoid bleeding complications before they start.
Additionally, we found that most patients (89%) were transferred from an outside hospital. Although we were not able to quantify the time from outside hospital admission to transfer, we suspect that the time was substantial and that there are even greater opportunities to improve the care of these patients by increasing ATRA availability at community hospitals, enhancing the education of all front-line providers regarding the prompt recognition of coagulopathy in the setting of suspected acute leukemia, and improving transfer center acceptance documentation that emphasizes the concern for APL and appropriate next steps in evaluation and treatment.

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Table 1: Demographic and Clinical Variables

Demographic and Clinical Variables	N=91
Age, *in years*	
Mean ± Standard Deviation	56.9 ± 18.0
Range	18.0 - 90.0
Gender, *n (%)*	
Female	41 (45.1%)
Male	50 (54.9%)
Ethnicity, *n (%)*	
White or Caucasian	55 (60.4%)
Black or African American	21 (23.1%)
Others or Unknown	15 (16.5%)
Admitted Through the Emergency Department, *n (%)*	
No	81 (89.0%)
Yes	10 (11.0%)
Admitted Overnight (1700-0700), *n (%)*	
No	12 (13.2%)
Yes	79 (86.8%)
ATRA Ordered Overnight (1700-0700), *n (%)*	
No	22 (24.2%)
Yes	69 (75.8%)
ATRA Administered Overnight (1700-0700), *n (%)*	
No	27 (29.7%)
Yes	64 (70.3%)
Fever Present Upon Admission, *n (%)*	
No	78 (85.7%)
Yes	13 (14.3%)
Signs or Symptoms of Bleeding Upon Admission, *n (%)*	
No	68 (74.7%)
Yes	23 (25.3%)
APL Diagnosis Prior to ATRA Administration, *n (%)*	
No	86 (94.5%)
Yes	5 (5.5%)
Diagnosed With APL, *n (%)*	
No	65 (71.4%)
Yes	26 (28.6%)

Demographic and Clinical Variables	N=91
Fresh Frozen Plasma Transfused During Admission, *units*	
Mean ± Standard Deviation	0.3 ± 0.9
Range	0.0 - 6.0
Platelets Transfused During Admission, *units*	
Mean ± Standard Deviation	9.4 ± 11.6
Range	0.0 - 59.0
Cryoprecipitate Transfused During Admission, *units*	
Mean ± Standard Deviation	1.0 ± 2.2
Range	0.0 - 13.0
Packed Red Blood Cells Transfused During Admission, *units*	
Mean ± Standard Deviation	6.4 ± 5.8
Range	0.0 - 33.0
White Blood Cell Count Upon Admission, *B/L*	
Mean ± Standard Deviation	55.3 ± 70.0
Range	0.7 - 355.6
Absolute Blast Count or Other Cell Count Upon Admission, *B/L*	
Mean ± Standard Deviation	33.0 ± 54.8
Range	0.0 - 352.0
Hemoglobin Upon Admission, *g/dL*	
Mean ± Standard Deviation	8.4 ± 1.9
Range	3.2 - 12.8
Platelet Count Upon Admission, *B/L*	
Mean ± Standard Deviation	53.3 ± 51.0
Range	4.0 - 244.0
Prothrombin Time Upon Admission, *seconds*	
Mean ± Standard Deviation	15.7 ± 2.6
Range	11.7 - 25.2
Partial Thromboplastin Time Upon Admission, *seconds*	
Mean ± Standard Deviation	28.7 ± 6.7
Range	18.0 - 67.0
Fibrinogen Upon Admission, *mg/dL*	
Mean ± Standard Deviation	308.6 ± 184.8
Range	47.0 - 792.0

Table 2: Time to ATRA and Univariate Linear Regression Analyses

Time Intervals	N=91
Time Interval A (Time from Admission to ATRA Order), *in minutes*	
Mean ± Standard Deviation	284.0 ± 274.6
Median ± IQR	187.0 ± 185.0
Skewness; Shapiro-Wilk	1.7
Range	22.0 - 1,227.0
Time Interval B (Time from ATRA Order to Administration), *in minutes*	
Mean ± Standard Deviation	103.7 ± 81.1
Median ± IQR	86.0 ± 105.5
Skewness; Shapiro-Wilk	1.5
Range	2.0 - 476.0
Time Interval C (Time from Admission to Administration), *in minutes*	
Mean ± Standard Deviation	387.7 ± 298.9
Median ± IQR	278.0 ± 234.0
Skewness; Shapiro-Wilk	1.5
Range	49.0 - 1,305.0

Variables for Time Interval A	Geometric mean ratio	Lower 95% CL	Upper 95% CL	P-value
Gender Male vs. Female	1.207	0.818	1.780	0.345
Age	1.006	0.995	1.017	0.263
Ethnicity Black vs. White	0.843	0.524	1.357	0.484
Ethnicity Others vs. White	1.112	0.648	1.909	0.701
Admitted through the emergency department Yes vs. No	1.319	0.710	2.448	0.383
Admitted overnight Yes vs. No	1.429	0.808	2.525	0.223
Fever Yes vs. No	1.229	0.707	2.138	0.466
Signs or symptoms of bleeding Yes vs. No	0.612	0.396	0.946	**0.030**
Log2(White Blood Cell Count)	1.016	0.937	1.101	1.744
Log2(Absolute Blast Count or Other Cell Count)	1.012	0.933	1.098	2.744
Hemoglobin upon admission (Hgb)	0.956	0.861	1.062	0.404
Platelet count upon admission (Plts)	1.001	0.997	1.005	0.636
Prothrombin time upon admission (PT)	1.040	0.966	1.120	0.305
Partial thromboplastin time upon admission (PTT)	0.993	0.964	1.022	0.624
Fibrinogen upon admission	1.001	1.000	1.002	0.164

Variables for Time Interval B	Geometric mean ratio	Lower 95% CL	Upper 95% CL	P-value
Gender Male vs. Female	1.273	0.857	1.889	0.235
Age	0.999	0.988	1.010	0.915
Ethnicity Black vs. White	0.704	0.436	1.139	0.157
Ethnicity Others vs. White	0.764	0.443	1.319	0.337
Admitted through the emergency department Yes vs. No	1.721	0.923	3.209	0.091
Admitted overnight Yes vs. No	1.048	0.584	1.881	0.876
ATRA ordered overnight Yes vs. No	0.977	0.615	1.552	0.923
Fever Yes vs. No	1.157	0.657	2.035	0.615
Signs or symptoms of bleeding Yes vs. No	0.803	0.510	1.263	0.344
Log2(White Blood Cell Count)	1.007	0.927	1.094	1.065
Log2(Absolute Blast Count or Other Cell Count)	1.014	0.933	1.101	2.065
Hemoglobin upon admission (Hgb)	1.020	0.917	1.135	0.715
Platelet count upon admission (Plts)	0.997	0.993	1.001	0.127
Prothrombin time upon admission (PT)	1.043	0.968	1.125	0.274
Partial thromboplastin time upon admission (PTT)	1.004	0.975	1.034	0.796
Fibrinogen upon admission	1.000	0.999	1.002	0.412

Figure 1

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