Table S1. IVIG indication and corresponding level of evidence[1,2]

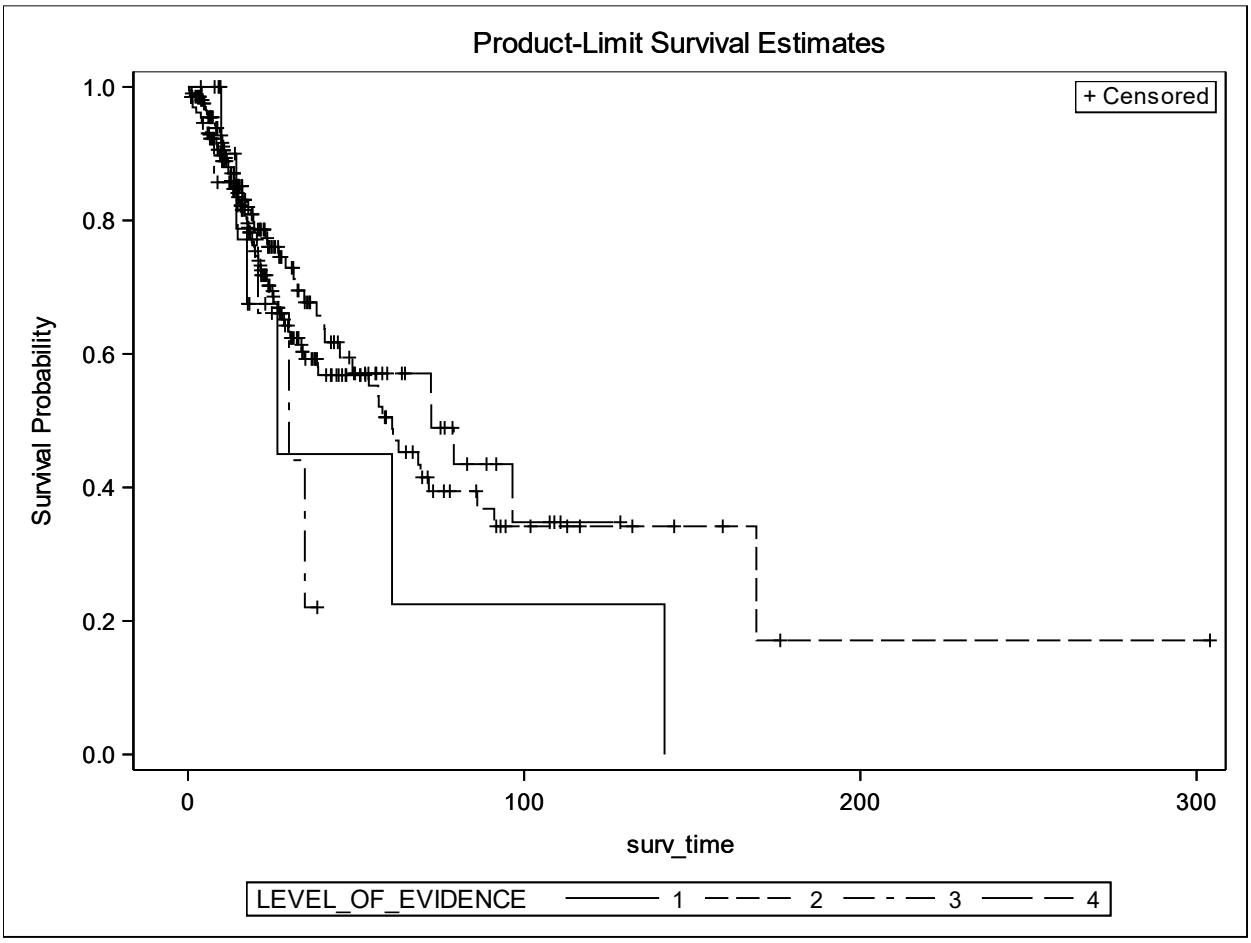
Level of Evidence	Indication	Non-Survivors, n (%) (n=139)	Survivors, n (%) (n=250)	Total, n (%) (N=389)
Level 1	Chronic inflammatory demyelinating polyneuropathy†	0 (0)	3 (1.2)	3 (0.8)
	BK virus cystitis	2 (1.4)	0 (0)	2 (0.5)
	Guillain-Barre Syndrome†	0 (0)	2 (0.8)	2 (0.5)
	Myasthenia gravis	2 (1.4)	5 (2.0)	7 (1.8)
	Cytomegalovirus pneumonia	1 (0.7)	0 (0)	1 (0.3)
Level 2	Hypogammaglobulinemia†	67 (48.2)	71 (28.4)	138 (35.5)
	Immune thrombocytopenic purpura†	10 (7.2)	42 (16.8)	52 (13.4)
	Common variable immunodeficiency	1 (0.7)	5 (2.0)	6 (1.5)
	Dermatomyositis†	1 (0.7)	4 (1.6)	5 (1.3)
	Polymyositis	0 (0)	4 (1.6)	4 (1.0)
	Systemic lupus erythematosus	1 (0.7)	2 (0.8)	3 (0.8)
	Sepsis	2 (1.4)	1 (0.4)	3 (0.8)
	Autoimmune encephalitis†	0 (0)	2 (0.8)	2 (0.5)
	Myositis	0 (0)	1 (0.4)	1 (0.3)
	Lambert-Eaton syndrome	0 (0)	1 (0.4)	1 (0.3)
	Factor V inhibitor	0 (0)	1 (0.4)	1 (0.3)
	Transverse myelitis	0 (0)	1 (0.4)	1 (0.3)
	Low IgA/IgM	0 (0)	1 (0.4)	1 (0.3)
Level 3	Respiratory syncytial virus	5 (3.6)	5 (2.0)	10 (2.6)
	Still's disease	1 (0.7)	3 (1.2)	4 (1.0)
Level 4	Lung transplant antibody mediated rejection†	14 (10.1)	46 (18.4)	60 (15.4)
	Toxic shock syndrome	6 (4.3)	10 (4.0)	16 (4.1)
	Hemolytic anemia	4 (2.9)	5 (2.0)	9 (2.3)
	Idiopathic thrombocytopenia	4 (2.9)	5 (2.0)	9 (2.3)
	Toxic epidermal necrolysis	1 (0.7)	6 (2.4)	7 (1.8)
	Stevens–Johnson syndrome	1 (0.7)	5 (2.0)	6 (1.5)
	Necrotizing fasciitis	4 (2.9)	1 (0.4)	5 (1.3)
	Hemophagocytic lymphohistiocytosis	4 (2.9)	1 (0.4)	5 (1.3)
	Aplastic anemia	1 (0.7)	2 (0.8)	3 (0.8)
	Capillary leak syndrome	2 (1.4)	1 (0.4)	3 (0.8)
	Hyperhemolysis	1 (0.7)	1 (0.4)	2 (0.5)
	Limbic encephalitis	1 (0.7)	1 (0.4)	2 (0.5)
	Parovirus	1 (0.7)	1 (0.4)	2 (0.5)
	Disseminated intravascular coagulation	0 (0)	1 (0.4)	1 (0.3)
	Heparin-induced thrombocytopenia	0 (0)	1 (0.4)	1 (0.3)
	Polychondritis	0 (0)	1 (0.4)	1 (0.3)
	Scleroderma	0 (0)	1 (0.4)	1 (0.3)
	Parainfluenza	0 (0)	1 (0.4)	1 (0.3)

	Drug-induced thrombocytopenia	0 (0)	1 (0.4)	1 (0.3)
	Autoimmune neutropenia	0 (0)	1 (0.4)	1 (0.3)
	Post transfusion purpura	0 (0)	1 (0.4)	1 (0.3)
	Catastrophic antiphospholipid syndrome	0 (0)	1 (0.4)	1 (0.3)
	Varicella zoster virus post-exposure prophylaxis	1 (0.7)	0 (0)	1 (0.3)
	Interstitial lung disease	1 (0.7)	0 (0)	1 (0.3)
	Hemolytic transfusion reaction	0 (0)	1 (0.4)	1 (0.3)
	Autoinflammatory syndrome	0 (0)	1 (0.4)	1 (0.3)

†Indication meets criteria for use per Cleveland Clinic formulary restrictions
p=0.06 for comparison of indication for IVIG between non-survivors and survivors

1. Group NICRW. https://www.blood.gov.au/ivig-criteria. Accessed October 2, 2018.
2. Care UKDoHaS. https://www.gov.uk/government/publications/clinical-guidelines-for-immunoglobulin-use-second-edition-update. Accessed October 2, 2018.

Figure S1. Survival analysis (Kaplan Meier plot and log rank test) for the four level of evidence groups



*Survival time (surv_time) = hospital length of stay

According to the p value (p = 0.37) in the log rank test, there are no significant differences at one or more points in survival time among the four level of evidence groups.

Figure S2. ROC curve for multivariate logistic regression model for overall population

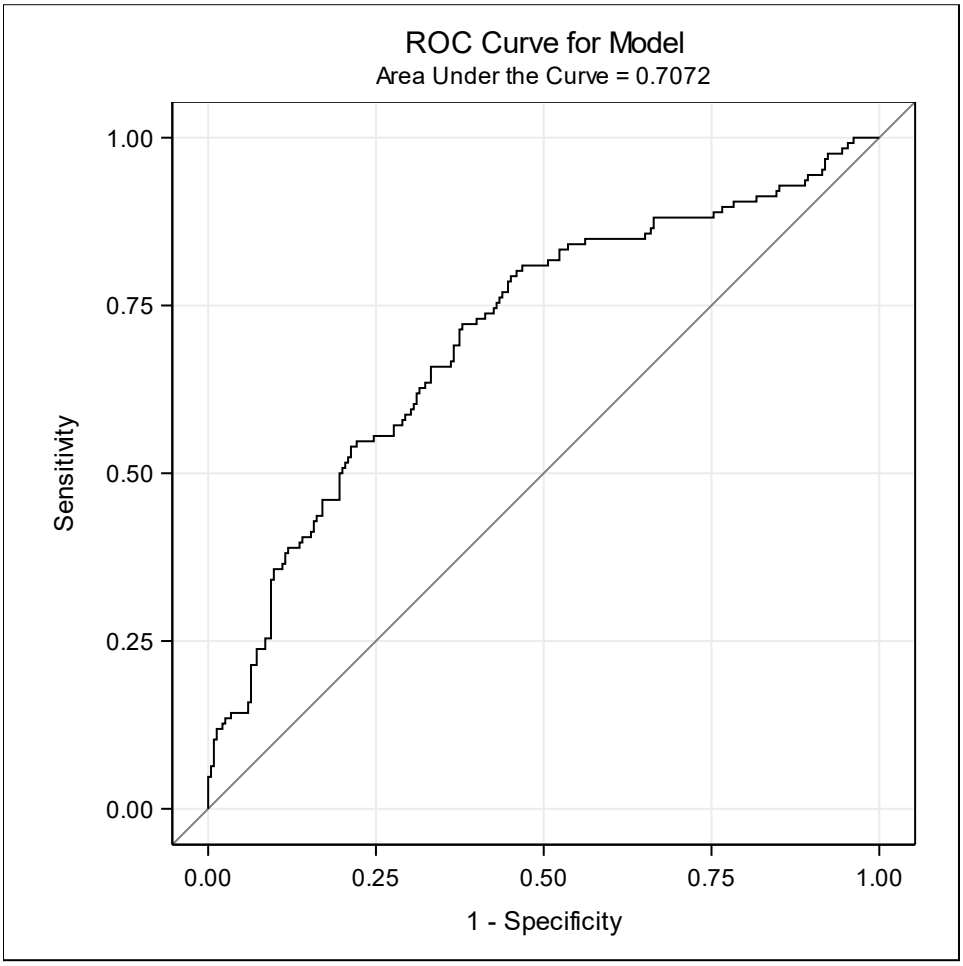


Table S2. IVIG utilization by patients with hypogammaglobulinemia

Variable	Non-Survivors (n=67)	Survivors (n=71)	P value
APACHE III score†	93.3 ± 30.9	80.4 ± 27.5	0.01[1]
IVIG dose, g‡	30 (25, 30)	30 (25, 30)	0.99[2]
IVIG dose, g/kg‡	0.4 (0.4, 0.4)	0.4 (0.4, 0.4)	0.007[2]
Total number of doses‡	1 (1, 1)	1 (1, 1)	0.64[2]
Cost per dose, USD‡	4893 (4077, 4893)	4893 (4077, 4893)	0.99[2]
Prior IVIG exposure, n (%)	24 (35.8)	28 (39.4)	0.66[3]
IgG level, mg/dL‡	374.5 (245.5, 426.0) (n=64)	373.0 (318.0, 432.0) (n=68)	0.39[2]
Lung transplant patients	9 (13.4)	14 (19.7)	0.32[3]
Days from admission to IVIG dose	6.4 ± 8.7	7.0 ± 7.2	0.24

†mean ± standard deviation, ‡Median (IQR), [1] Equal Variance T-Test, [2] Wilcoxon, [3] Chi-Square test

APACHE: acute physiology and chronic health evaluation; IVIG: intravenous immune globulin

Table S3. IVIG utilization by lung transplant patients for antibody mediated rejection

Variable	Non-Survivors (n=14)	Survivors (n=46)	P value
APACHE III score†	67.8 ± 28.6 (n=13)	66.8 ± 20.8 (n=44)	0.89[1]
IVIG dose, g†	67.5 ± 11.6	64.2 ± 17.2	0.51[1]
IVIG dose, g/kg‡	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	0.35[2]
Total number of doses‡	2.5 (2.0, 4.0)	2.0 (1.0, 3.0)	0.40[2]
Cost per dose, USD†	11009 ± 1886	10477 ± 2799	0.51[1]
Prior IVIG exposure, n (%)	9 (64.3%)	28 (60.9%)	0.82[3]

†mean ± standard deviation, ‡Median (IQR), [1] Equal Variance T-Test, [2] Wilcoxon, [3] Chi-Square test
APACHE: acute physiology and chronic health evaluation; IVIG: intravenous immune globulin

Table S4. IVIG utilization by patients with hematologic indications

Variable	Non-Survivors (n=24)	Survivors (n=67)	P value
APACHE III score†	84.9 ± 33.5 (n=22)	66.9 ± 28.6 (n=63)	0.02[1]
IVIG dose, g‡	30.0 (25.0, 50.0)	45.0 (25.0, 65.0)	0.14[2]
IVIG dose, g/kg‡	0.5 (0.4, 1.0)	0.6 (0.4, 1.0)	0.16[2]
Total number of doses‡	2.0 (1.0, 2.5)	2.0 (1.0, 3.0)	0.29[2]
Cost per dose, USD‡	4893 (4077, 8155)	7339 (4077, 10601)	0.14[2]
Prior IVIG exposure, n (%)	6 (25%)	17 (25.4%)	0.97[3]

†mean ± standard deviation, ‡Median (IQR), [1] Equal Variance T-Test, [2] Wilcoxon, [3] Chi-Square test
APACHE: acute physiology and chronic health evaluation; IVIG: intravenous immune globulin

Hematologic indications included in the analysis: aplastic anemia, autoimmune hemolysis, autoimmune neutropenia, common variable immunodeficiency, disseminated intravascular coagulation, Factor V inhibitor, hemolytic anemia, hemolytic transfusion reaction (sickle cell), hemophagocytic lymphohystiocytosis, heparin induced thrombocytopenia, hyperhemolysis, immune thrombocytopenia purpura, low IgM/IgA, pancytopenia, thrombocytopenia

Table S5. Subgroup multivariate logistic regression

	Odds Ratio	95% Confidence Interval	P value
Hypogammaglobulinemia			
Female vs Male	0.394	(0.158, 0.986)	0.0465
Age (1 year increase)	0.986	(0.959, 1.014)	0.3313
APACHE III score (1 unit increase)	1.018	(1.004, 1.032)	0.0115
Dose (1 g/kg increase)	0.104	(0.004, 2.458)	0.1609

Weight (1 kg increase)	0.998	(0.975, 1.021)	0.8458
Lung transplant antibody mediated rejection			
Female vs Male	2.073	0.437 – 9.821	0.3585
Age (1 year increase)	1.002	0.955 – 1.052	0.9227
APACHE III score (1 unit increase)	1.010	0.978 – 1.043	0.5505
Dose (1 g/kg increase)	7.879	0.154 – 403.473	0.3040
Weight (1 kg increase)	1.044	0.984 – 1.108	0.1543
Hematologic indications			
Female vs Male	0.759	0.247 – 2.331	0.6307
Age (1 year increase)	1.001	0.969 – 1.034	0.9446
APACHE III score (1 unit increase)	1.016	0.998 – 1.035	0.0765
Dose (1 g/kg increase)	0.338	0.049 – 2.354	0.2734
Weight (1 kg increase)	0.986	0.959 – 1.014	0.3177
Severely ill patients with an APACHE III score of ≥ 80			
Female vs Male	0.728	0.339 – 1.565	0.4166
Age (1 year increase)	0.995	0.972 – 1.019	0.6823
APACHE III score (1 unit increase)	1.023	1.007 – 1.038	0.0038
Dose (1 g/kg increase)	0.291	0.085 – 1.001	0.0502
Weight (1 kg increase)	1.013	0.994 – 1.033	0.1786
Non severely ill patients with an APACHE III score of < 80			
Female vs Male	0.446	0.213 – 0.932	0.0319

Age (1 year increase)	1.016	0.993 – 1.039	0.1647
APACHE III score (1 unit increase)	0.996	0.975 – 1.018	0.7481
Dose (1 g/kg increase)	0.296	0.094 – 0.932	0.0376
Weight (1 kg increase)	0.985	0.966 – 1.004	0.1214

APACHE: acute physiology and chronic health evaluation

Figure S3. ROC curve for hypogammaglobulinemia subgroup multivariate logistic regression model

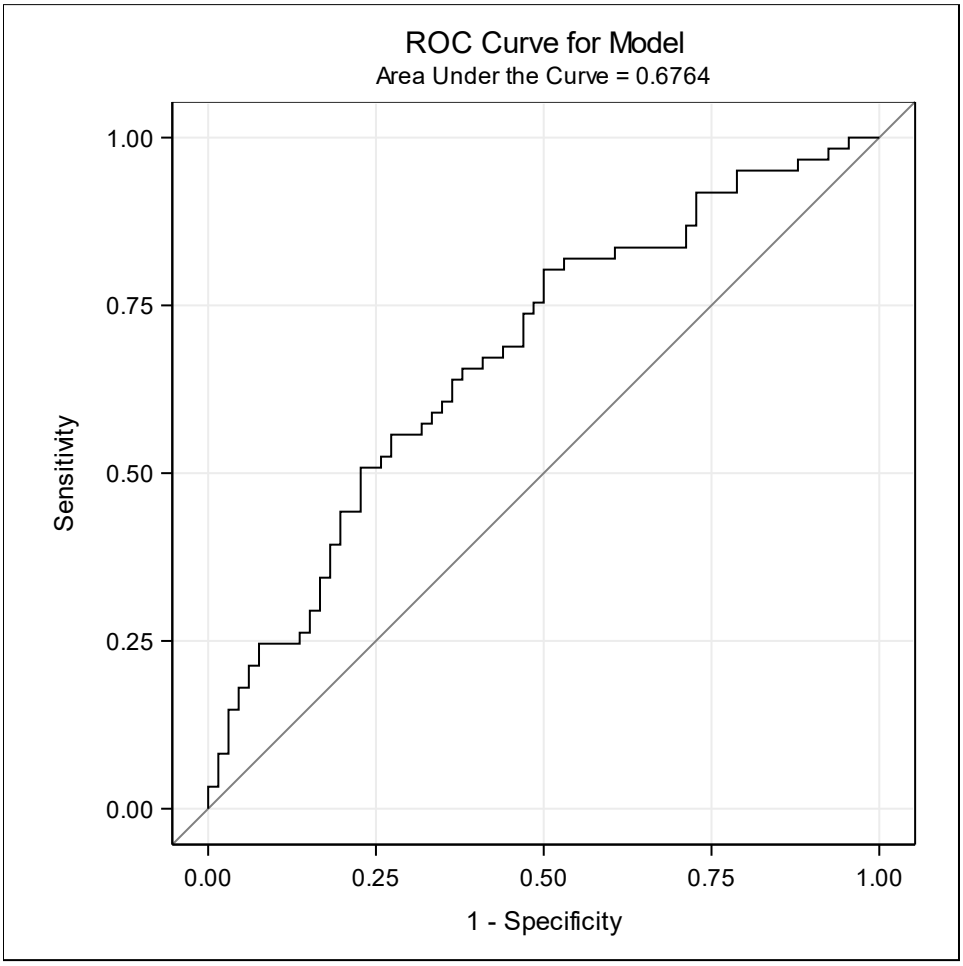


Figure S4. ROC curve for lung transplant antibody mediated rejection subgroup multivariate logistic regression model

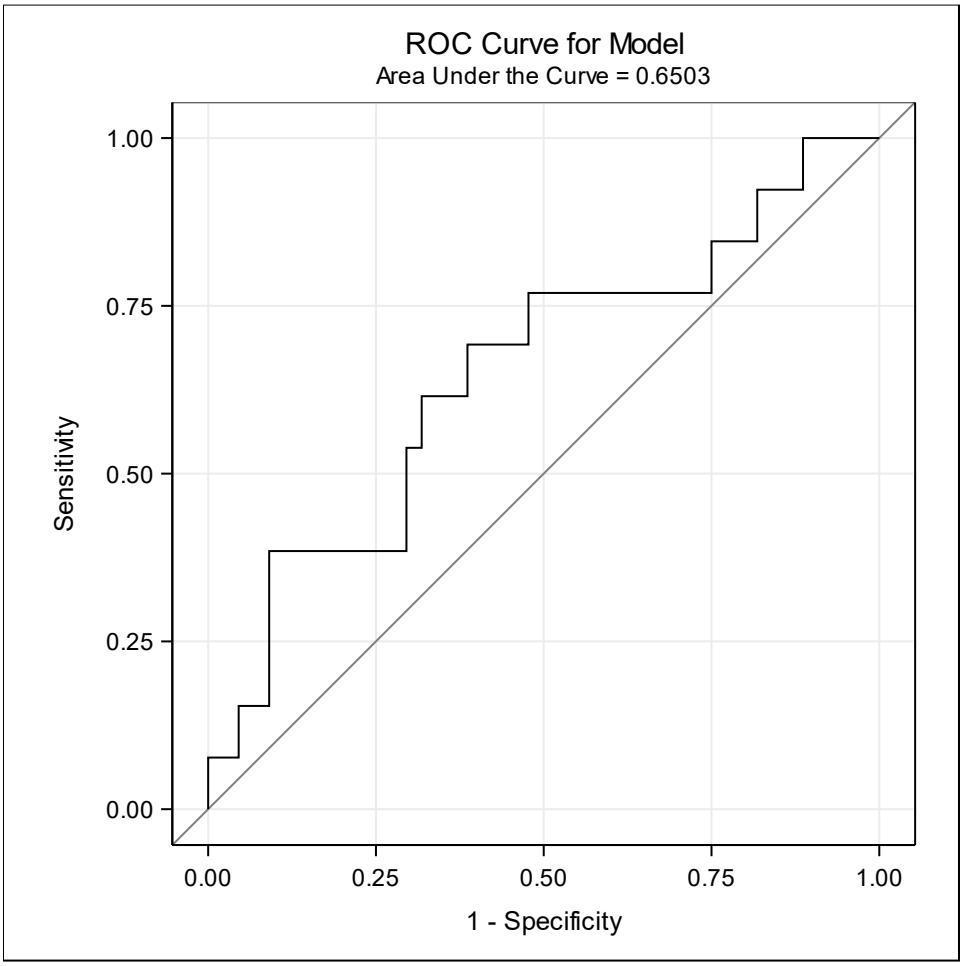
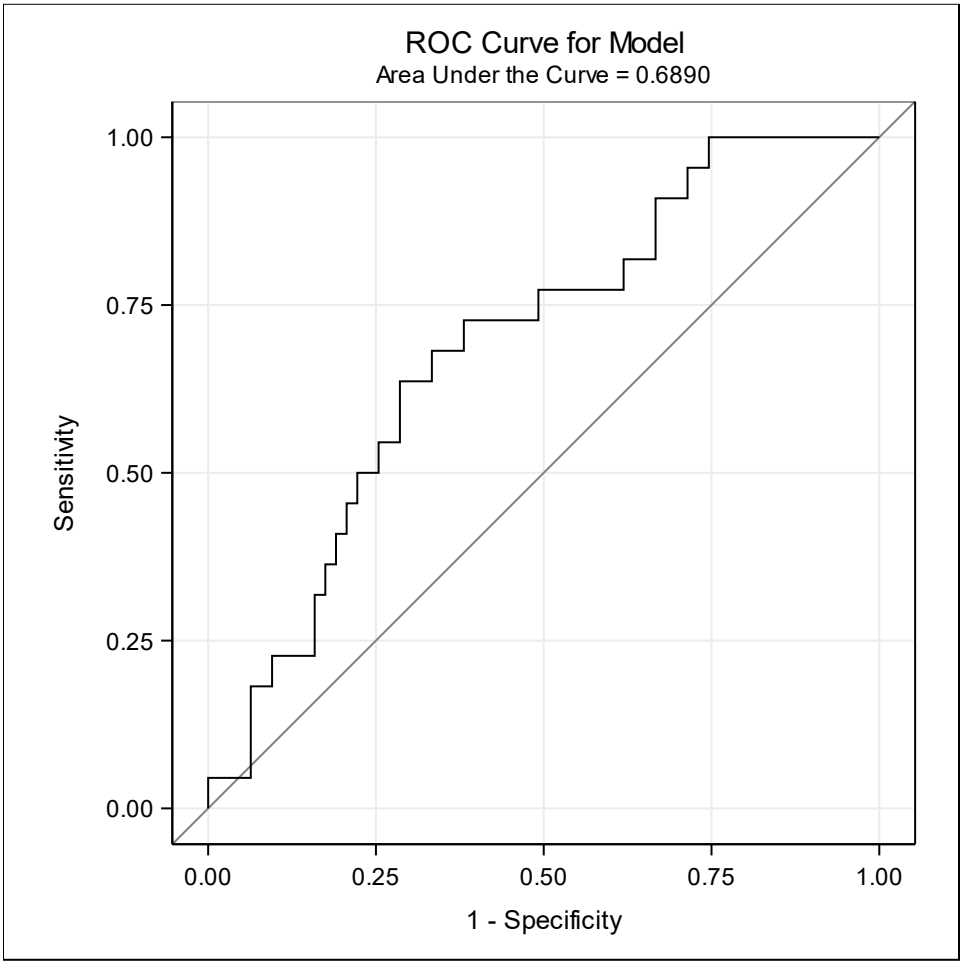



Figure S5. ROC curve for hematologic indications subgroup multivariate logistic regression model