

Supplemental Table 3. Large series (n>50) including adult HLH patients with unselected etiologies

Author	Year	Country	Patients	Admission	Etiologies	Mortality		Prognostic factors		Outcomes	Main outcome analysis	
						Early	Overall	Univariate	Multivariate	Primary (secondary)	Univariate	Multivariate
Buyse	2010	France	56	ICU	Tumoral diseases (77%) Infections (41%) Undetermined (7%)	39% (ICU)	52% (Hospital)	SOFA scores, platelet count, hemophagocytosis, shock at ICU admission, life-sustaining therapies, Castleman's disease, B cell lymphoma	Shock at ICU admission, platelet count (risk factor) Castleman's disease and B-cell lymphoma (protective factor)	Hospital mortality (died in the ICU or before hospital discharge)	Chi-square test or Fisher's exact test (categorical variables) Wilcoxon or Kruskal-Wallis test (continuous variables)	Logistic regression model (forward stepwise selection procedure using all variables associated with hospital mortality in the univariate analysis)
Barba	2015	France	71	ICU	Neoplasia (30%) Infection (28%) Autoimmune disease (10%) HLH of unknown origin (26%)	38% (28-day)	68% (Hospital)	Age, SOFA scores (the 28-day mortality) Age, SOFA scores, lymphoma related HLH or HLH of unknown origin, thrombocytopenia, need for renal replacement therapy (hospital mortality)	Age, SOFA scores (the 28-day mortality) Age, SOFA scores, lymphoma related HLH or HLH of unknown origin, thrombocytopenia (hospital mortality)	28-day mortality (hospital mortality)	Chi-square test or Fisher's test (categorical variables) The Mann-Whitney U nonparametric test (continuous variables)	Binary logistic regression (backward stepwise selection method using all variables associated with a p-value <0.10 in the univariate analysis)
Li	2014	China	103	Hospital	Hematologic malignancies (48%) Infectious disease (23%) Autoimmune diseases (14%) Unknown origin (23%)	ND	75% (Overall)	Age at disease onset, male sex, splenomegaly, thrombocytopenia	Male sex	Overall mortality	Pearson's chi-square test (categorical variables) Mann-Whitney U test (quantitative variables).	Multivariate logistic regression
Valade	2015	France	117	ICU	Hematologic conditions (73%) Infectious diseases (20%) Systemic diseases (5%) Undetermined HLH etiology (2%)	28% (ICU)	44% (Hospital)	Fibrinogen level <2 g/L, age >46 years, SOFA scores, worst PT	Fibrinogen level <2 g/L, age >46 years, SOFA scores	Coagulation disorders (hospital mortality)	Fisher's exact test (categorical variables) Wilcoxon rank-sum tests (continuous variables) Kaplan-Meier (Survival according to the fibrinogen level, prothrombin time, SOFA score)	Logistic regression model (backward stepwise procedure using all variables yielding p-values<0.20 in the univariate analysis)

Otrock	2015	US	73	Hospital	<p>Malignancy (29%)</p> <p>Infection (41%)</p> <p>Autoimmunity (7%)</p> <p>Unknown (18%)</p>	27% (30-day)	52% (Overall)	<p>Male gender, age≥30 years, renal insufficiency, percent drop in serial ferritin of <75%, malignancy-associated causes of HLH (overall mortality)</p>	<p>Malignancy-associated causes of HLH (overall mortality)</p> <p>Ferritin level> 50,000 mg/L (30-day mortality)</p>	Overall mortality (30-d mortality)	<p>Pearson's Chi-square or Fisher's exact test (categorical variables)</p> <p>Student's t-test (continuous variables)</p> <p>Kaplan-Meier (Survival according to the malignancy-associated HLH)</p>	<p>Logistic regression (backward step-wise (Wald) selection procedure with significance level for removal from the model set at 0.1)</p>
Riviere	2015	France	162	Hospital	<p>Hematologic malignancies/Solid cancer (60%)</p> <p>Infections (25%)</p> <p>Systemic disease (3%)</p> <p>Other/unknown underlying disease (9%)</p>	20% (30-day)	42% (Overall)	<p>Hematologic malignancy-associated hemophagocytic syndrome has a poorer outcome than those with underlying infection</p>		Thirty-day mortality	<p>Kaplan-Meier (survival was compared between hematologic malignancies-associated and infection-associated hemophagocytic syndrome using the log-rank test)</p>	
Zhou	2017	China	205	Hospital	<p>Malignancies (58%)</p> <p>Infections (41%)</p> <p>Autoimmune disorders (7%)</p> <p>Unknown (7%)</p>	43% (30-day)	64% (Overall)		<p>Platelet, prothrombin time and malignancy (all patients)</p> <p>Direct bilirubin (elderly group)</p> <p>Prothrombin time,malignancy and lactate dehydrogenase (young group)</p>	Overall mortality	<p>Pearson's Chi-square and non-parametric tests (categorical variables)</p> <p>Mann-Whitney U test (continuous variables)</p> <p>Kaplan-Meier (Survival curves)</p>	Cox-regression method
Schram	2016	US	68	Hospital	<p>Malignancy (49%)</p> <p>Infection (33%)</p> <p>Autoimmune disease (28%)</p>	21% (30-day)	69% (Overall)	<p>Malignancy-associated HLH had a worse survival compared to those without underlying cancer. There was a trend towards improved survival in patients who received etoposide.</p>		Overall mortality	<p>Kaplan-Meier (survival analyses to compare subgroups using the log-rank test)</p>	