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Outcomes of Adult and Pediatric Patients with Hematologic Malignancies and COVID-19: A Systematic Review and Meta-Analysis of 1847 Patients

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**Introduction:** Clinical outcomes for patients with hematologic malignancy and COVID-19 have not been aggregated. We completed a systematic review and meta-analysis to estimate the risk of death and other important outcomes for these patients.

**Methods:** We searched Pubmed and EMBASE up to July 25, 2020, to identify reports of patients with hematologic malignancy and COVID-19 (including papers where the patients with hematologic malignancy were a subset of the total study population). The primary outcome was a pooled mortality estimate, considering all patients and only hospitalized patients. Secondary outcomes included pooled estimates for the risk of ICU admission, mechanical ventilation, and non-invasive ventilation in hospitalized patients.

Mortality data were stratified by age, treatment status, and malignancy subtype. For treatment status, "systemic anti-cancer therapy (SACT)" was defined as patients on any anti-cancer therapy. "Cytotoxic SACT" was defined as patients on cytotoxic therapy only. "Not on treatment" was defined as patients on observation or those who were at least 28 days beyond their last active treatment.

Sensitivity analyses were conducted on the primary outcomes limiting to studies with low risk of bias, and to studies including both outpatients and hospitalized patients. Due to data limitations, only the primary outcome was assessed for pediatric studies. Pooled prevalence and risk ratios (RR) and 95% confidence intervals (CI) were calculated using a random-effects model using MetaXL and Revman 5.4 software.

**Results:** A total of 25 adult studies and 4 pediatric studies comprising 1847 patients from China, Europe, the United Kingdom, and North America were included (Figure 1 and Table 1). The majority of patients were hospitalized (83%). The overall risk of death amongst all patients was 36% (95% CI 31-41, N=1763), and amongst hospitalized patients was 40% (95% CI 36-45, 24 studies with 1295 patients) (Figure 2). Patients aged >60 years had a significantly higher risk of death than patients <60 years (46% vs. 26%, RR 1.56, 95%CI 1.15-2.13, N=597) (Figure 3). The pooled risk of death in pediatric patients was 4% (95% CI 1-9, N=102) (Figure 2).

The risk of ICU admission among hospitalized adult patients was 23% (95% CI 17-29, N=1165); mechanical ventilation 16% (95% CI 12-21, N= 826); and non-invasive ventilation 16% (95% CI 9-26%, N=373).
The estimated RR of death among patients on SACT compared to no treatment was 1.22 (95% CI 0.84-1.78; N=457, Figure 3a). The RR of death among patients on cytotoxic SACT versus no treatment was similar at 1.29 (95% CI 0.78-2.15; N=176, Figure 3b).

All subgroups of hematologic malignancy had high risks of overall mortality: acquired bone marrow dysfunction syndromes 57% (95% CI 42-72, 11 studies, 42 patients); leukemias 44% (95% CI 31-58, 15 studies, 159 patients), plasma cell dyscrasias 38% (95% CI 29-47, 18 studies, 387 patients); lymphomas (including CLL) 32% (95% CI 26-38, 16 studies, 696 patients); lymphomas (excluding CLL) 32% (95% CI 18-48, 11 studies, 156 patients); CLL 31% (95% CI 24-39, 13 studies, 457 patients); myeloproliferative neoplasms 37% (95% CI 25-49, 9 studies, 62 patients).

Sensitivity analysis including only studies with a low risk of bias showed a similar estimate for risk of death among all patients (37% (95% CI 31-42, 20 studies with 1412 patients)) compared to all studies. Sensitivity analysis including only studies reporting on a combination of outpatients and hospitalized patients also showed a similar estimate for risk of death among all patients (38% (95% CI 32-44), 11 studies with 1214 patients) compared to all studies.

**Conclusion:** Adult patients with hematologic malignancy and COVID-19, especially hospitalized patients, appear to experience a high risk of dying (pooled risk estimate 36%). Older patients experience higher mortality, and pediatric patients appear to be relatively spared. Importantly, based on the observational data available to date, recent cancer treatment does not appear to significantly increase the risk of dying. These data highlight the need for robust strategies to prevent patients with hematologic malignancy from
contracting COVID-19, and may help inform discussions about prevention strategies, treatment, and goals of care.
Disclosures

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