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Research paper

Sharing post-AML consolidation supportive therapy with local centers reduces patient travel burden without compromising outcomes

Samantha A. Hershenfeld, Kimberly Maki, Lana Rothfels, Cindy S. Murray, Shannon Nixon, Aaron D. Schimmer, Mary C. Doherty*

Princess Margaret Cancer Center, University Health Network, 610 University Ave, Toronto, Ontario, Canada M5G 2M9

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ABSTRACT

Acute myeloid leukemia (AML) is frequently treated with induction and consolidation chemotherapy. Consolidation chemotherapy can be delivered on an ambulatory basis, requiring some patients to travel long distances for treatment at specialized centers. We developed a shared care model where patients receive consolidation chemotherapy at a quaternary center, but post-consolidation supportive care at local hospitals. To evaluate the impact of our model on patient travel and outcomes we conducted a retrospective analysis of AML and acute promyelocytic leukemia patients receiving consolidation over four years at our quaternary center. 73 patients received post-consolidation care locally, and 344 at the quaternary center. Gender, age and cytogenetic risk did not significantly differ between groups. Shared care patients saved mean round trip distance of 146.5 km ± 99.6 and time of 96.7 min ± 63.4 compared to travelling to quaternary center. There was no significant difference in overall survival between groups, and no increased hazard of death for shared care patients. 30, 60, and 90 day survival from start of consolidation was 98.6%, 97.2%, and 95.9% for shared care and 98.8%, 97.1%, and 95.3% for quaternary center patients. Thus, a model utilizing regional partnerships for AML post-consolidation care reduces travel burden while maintaining safety.

1. Introduction

The mainstay of treatment for acute myeloid leukemia (AML) is induction and consolidation chemotherapy. These treatments produce periods of pancytopenia requiring supportive care including blood count monitoring, transfusion support, and treatment of infections [1]. While induction chemotherapy is typically administered as an in-patient therapy, consolidation chemotherapy is increasingly being delivered on an ambulatory basis. When patients are monitored post consolidation chemotherapy as out-patients, they return to clinic once to twice per week during the period of pancytopenia that lasts approximately 3–4 weeks [1–3]. Most patients receive 2–4 cycles of consolidation chemotherapy [4–6].

Our group and others have demonstrated the safety of outpatient consolidation chemotherapy for selected patients [1,7–13]. However, ambulatory care during outpatient consolidation chemotherapy is often centralized at quaternary centers with large catchment areas. As a result, some patients are required to travel long distances for their frequent out-patient appointments. These long travel distances could negatively impact quality of life and create a barrier to care.

To address the issue of long distances of travel, the Princess Margaret Cancer Center, a quaternary care cancer center in Toronto, Canada developed and implemented a model of care where patients receive their post-consolidation supportive therapy, including blood count monitoring, transfusions, and management of febrile neutropenia at their local hospitals while the consolidation chemotherapy itself is administered at the quaternary care center. Here, we review the impact of the shared care model with an emphasis on travel time and distance saved.

2. Materials and methods

2.1. Study design

We conducted a retrospective cohort analysis and compared patients who received post-consolidation supportive care at their local hospitals between 2009–2013 as part of the shared care model to patients who did not participate in this model and received their post-consolidation supportive care at the quaternary center during the same timeframe. Both groups of patients received induction and consolidation chemotherapy at the quaternary care center. All patients included had a diagnosis of AML or acute promyelocytic leukemia (APL), and

* Corresponding author.
E-mail address: Mary.Doherty@uhn.ca (M.C. Doherty).

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were receiving post-consolidation care in first complete remission (CR1).

Patients were selected for the shared care model by specialized oncology nurse coordinators, oncology nurse practitioners, and staff attending physicians based on geographic distance from the quaternary center using the patient's home address. Patient participation in the shared care model was encouraged but not mandatory. Partnerships with regional hospitals were established through communication and training between the hematologists/oncologists, nurse coordinators, and nurse practitioners at the quaternary center and partner sites. Annual education days were held at both partner sites and the quaternary center to review supportive care protocols and support the multidisciplinary teams at the local hospitals. Regional hospitals were staffed by medical oncologists, hematologists, and/or nurse practitioners, with experience in the treatment of cytopenias and febrile neutropenia. Patients were seen at least weekly on an ambulatory basis at these centers while recovering from consolidation chemotherapy. All regional hospitals in the model had transfusion and intensive care capabilities.

For each patient enrolled in the shared care model, the quaternary center sent a request letter with guidelines for partner sites (Appendix A in Supplementary material). These guidelines included specific instructions regarding frequency of blood count checks, transfusion thresholds, central venous access device (CVAD) maintenance, and symptom management including febrile neutropenia. Patients were also given a copy of this letter and encouraged to bring this with them to all visits at their local centers. In addition to the guidelines above, the letter lists the name of his or her most responsible physician at the quaternary center. Current on-call rosters were published for timely physician–physician communication between sites.

Guidelines for transfusion support recommended prophylactic packed red blood cells to maintain a hemoglobin above 80 g/L and an adult dose of platelets to maintain a platelet count above 10×10^9/L. For active bleeding, it was recommended to keep platelets > 20, or > 50 with severe bleeding. The request letter also indicated whether irradiated or HLA matched products were required.

Instructions for treatment of febrile neutropenia were detailed in the request letter sent to local centers. The recommended protocol included performing blood cultures through each central venous port and peripherally, immediately starting IV antibiotics, and admitting the patient to hospital. Local sites were advised to contact the nursing coordinator or most responsible physician at the quaternary center to inform them of the admission. Patients were treated for febrile neutropenia at the local center, and only transferred to the quaternary center in the case of a recurrence or for complications as needed. The recommended treatment was piperacillin/tazobactam 4.5 g IV every 8 h, plus tobramycin or gentamicin 5 mg/kg IV every 24 h.

Consolidation chemotherapy regimen for AML patients included 2-3 cycles of cytarabine 3 g/m^2 (patients < 60 years) or 1.5 g/m^2 (> 60 years old) per dose IV over 3 h q12 h on Days 1, 3, 5 (6 doses total) with or without daunorubicin 45 mg/m^2 daily × 2 (for EF > 50% or < 10% drop between cycles) and APL patients received 2 cycles of consolidation, the first of which consisted of ATRA 45 mg/m^2/day in 2 divided doses × 28 days, daunorubicin 60 mg/m^2/day on days 1, 2, 3, and cytarabine 100 mg/m^2/day continuous IV infusion × 7 days, on days 1–7. ATRA 45 mg/m^2/day in 2 divided doses × 28 days, daunorubicin 45 mg/m^2/day on days 1, 2, 3, and cytarabine 1.5 g/m^2 q12 h × 6 doses on days 1, 3 and 5 were given for the second consolidation cycle.

All patients received antibacterial (ciprofloxacin and amoxicillin), antifungal (fluconazole) and antiviral (acyclovir) prophylaxis during chemotherapy.

2. Outcome measurements

Travel distance and estimated travel time from patients' home address to their local regional center or quaternary center (Princess Margaret) was calculated using postal codes and Google Maps (www.google.ca/maps). Of note, prior studies on the Canadian postal codes demonstrated that this measure localizes the location to within 200 and 500 m of the true address in 88 and 96% of cases, respectively [14]. Times and distances were calculated using the shortest distance by automobile and the use of toll roads was permitted. The Kaplan-Meier method was used to estimate overall survival (OS), and survival differences were analyzed by the log-rank test. Research ethics board approval for this study was granted by the University Health Network.

3. Results

3.1. Model of care

During the timeframe evaluated, seventy-three patients with either AML (n = 61) or APL (n = 12) received post-consolidation therapies at local hospitals as part of the shared care model, and three hundred and forty-four patients with AML (n = 297) or APL (n = 47) received all their care at the quaternary center. Of shared care patients, 54.8% were male, and the median age was 57 years. Favourable, intermediate and poor risk cytogenetics were identified in 9.6%, 57.5%, and 8.2% of shared care patients, respectively, according to Southwest Oncology Group (SWOG) criteria. No significant differences were found between the demographic and cytogenetic characteristics of the shared care and quaternary care groups (Table 1).

Shared care patients underwent a total of 137 cycles of consolidation chemotherapy, which were administered at the quaternary center. However, for each cycle, post-consolidation supportive care was delivered at fourteen regional hospitals in the province of Ontario, Canada, situated a median distance of seventy kilometers (range: 36–190) from the quaternary site. Each local site treated a median of 2 patients (range: 1–19 patients).

3.2. Travel time and distance

Mean travel distance and time were significantly reduced for shared care patients travelling to their local hospitals compared to commuting from their homes to the quaternary center ($p = 3.81 \times 10^{-20}$ and $p = 6.28 \times 10^{-21}$ for difference in means by *t*-test for distance and time travelled, respectively) (Fig. 1a & b).

Median distance and time were 87.8 km (range: 28.4–266) and 62 min (range: 29–170), respectively, one way from patients' homes to the quaternary center, versus a median 14.5 km (range: 0.55–211) and 18 min (range: 2–137) to their local centers.

3.3. Survival

Survival measured from the start of consolidation chemotherapy was found to be 98.6%, 97.2%, and 95.9%, for patients in the shared care model at 30, 60 and 90 days, respectively. For the group who

Table 1
Patient characteristics.

	Shared Care	Quaternary Care Center	P value
n	73	344	
Median age (range)	56.99 (21.7–78.6)	55.38 (18.5–85.8)	0.37
Gender (n, %male)	40 (54.8%)	167 (48.5%)	0.4
APL (n, %)	12 (16.44%)	47 (13.67%)	0.67
Cytogenetics (n, %)			0.7
Good	7 (9.6%)	35 (10.17%)	
Intermediate	42 (57.53%)	208 (60.46%)	
Poor	6 (8.22%)	36 (10.46%)	
Unknown	18 (24.65%)	65 (18.89%)	

Difference in means calculated by *t* test. Difference in categorical variables calculated by chi square test.