Journal of Pediatric Surgery (2013) **48**, 1254–1262

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Journal of Pediatric Surgery

www.elsevier.com/locate/jpedsurg

Wilms tumor survival in Kenya

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Received 15 February 2013; accepted 8 March 2013

Key words:
Wilms tumor;
Global health;
Pediatric cancer;
Kenya;
Race disparity

Abstract

Purpose: Survival from Wilms Tumor (WT) exceeds 90% at 5 years in developed nations, whereas at last report, 2-year event-free survival (EFS) in Kenya reached only 35%. To clarify factors linked to these poor outcomes in Kenya, we established a comprehensive web-based WT registry, comprised of patients from the four primary hospitals treating childhood cancers.

Materials and methods: WT patients diagnosed between January 2008 and January 2012 were identified. Files were abstracted for demographic characteristics, treatment regimens, and enrollment in the Kenyan National Hospital Insurance Fund (NHIF). Children under 15 years of age having both a primary kidney tumor on imaging and concordant histology consistent with WT were included.

Results: Two-year event-free survival (EFS) was 52.7% for all patients (n = 133), although loss to follow up (LTFU) was 50%. For the 33 patients who completed all scheduled standard therapy, 2-year EFS was 94%. Patients enrolled in NHIF tended to complete more standard therapy and had a lower hazard of death (Cox 0.192, $p < 0.001$).

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http://dx.doi.org/10.1016/j.jpedsurg.2013.03.021

Conclusion: Survival of Kenyan WT patients has increased slightly since last report. Notably, WT patients completing all phases of standard therapy experienced 2-year survival approaching the benchmarks of developed nations. Efforts in Kenya should be made to enhance compliance with WT treatment through NHIF enrollment.

Nephroblastoma or Wilms Tumor (WT) is the most common childhood kidney cancer worldwide, yet its incidence, behavior, and outcome vary according to ethnicity and geographic location[1]. WT poses a disease burden to black sub-Saharan Africans and ranks second or third among the most frequently diagnosed childhood cancers [2,3]. This frequency differs from North American childhood cancer incidences, which place WT fifth behind leukemia, lymphoma, CNS tumors, and neuroblastoma [4].

Although WT is often curable in developed nations, children affected in resource-constrained regions of Sub-Saharan Africa experience poor outcomes. Kenya is one such country particularly burdened by this childhood cancer[5]. The last analysis of WT survival among Kenyan patients reported a two-year event-free survival (EFS) of only 34.7% [6], which stands in contrast to recent survival rates exceeding 90% at 5 years in developed countries [7,8]. WT therefore occurs commonly among Kenyan children and continues to produce an unacceptably high mortality.

Interestingly, this increased predisposition for children of black African ancestry to develop WT persists despite geographic location and generations of genetic distance from sub-Saharan origin. Black African-American children have an increased incidence of WT (11 cases per million children <15 y of age) compared with whites (8 cases per million) [1,9]. Among children presenting with WT in Tennessee, a greater proportion were black, and differences in molecular profiling of WT were observed between race groups, which may in part contribute to these ethnic variations in both incidence and outcome [10,11].

Curious about the possibility of a biological basis for these disparities, we recently conducted an exploratory study to characterize the molecular phenotype in Kenyan Wilms Tumor (KWT) [11]. KWT specimens showed many of the classical and typical features of WT. Disease aggressiveness, treatment resistance, and a distinct molecular signature suggested a unique tumor phenotype in these patients. However, interpretation of these results was limited by high numbers of patients who became lost to follow up or abandoned care; in addition, clinical data were incomplete in nearly every case. Sample sizes were too small to make generalizable statements.

To refine and clarify the clinical significance of these preliminary molecular observations, a partnership was established between researchers at Vanderbilt University Medical Center (VUMC), Meharry Medical School in Nashville TN, and the four highest volume pediatric surgical hospitals in Kenya: Kenyatta National Hospital (KNH) in Nairobi, AIC Kijabe Hospital in Kijabe, Tenwek Mission Hospital in Bomet, and Moi Teaching and Referral Hospital (MTRH) in Eldoret. The purposes of these collaborations are: 1) to create a comprehensive Kenyan WT registry (KWTR) for gathering clinical data and for facilitating ongoing patient treatment; 2) to create a WT tissue repository for parallel biological studies, and 3) to assign molecular profiles more reliably to those WT patients having completed cancer care, which will yield greater prognostic accuracy than the alternative and less precise scenario if patients remain undertreated.

We hypothesized that event-free survival (EFS) for children diagnosed with and treated for WT had improved since last report, but that a higher death rate from WT would persist when compared to that in more developed countries. Secondarily, we hypothesized that completion of all phases of therapy would result in greater EFS and that greater access to care through national health insurance coverage would improve completion of therapy and thereby decrease the risk of death.

1. Materials and methods

1.1. Study design and definitions

To initiate the KWTR, we performed a retrospective chart review of all patients diagnosed with WT beginning January 1, 2008. All patients under 15 years of age having imaging or operative findings of a primary kidney tumor were included. We excluded patients with a pathologic diagnosis of a tumor other than WT. Several definitions are important to understand this study. Loss to follow-up (LTFU) was defined as any patient missing his or her next scheduled treatment or follow-up appointment and further not having a scheduled follow-up appointment. Study patients were classified as active in therapy if currently receiving chemotherapy, radiation therapy, or surgical planning and who were not LTFU. Patients were classified as having completed all therapy if all therapeutic interventions, including preoperative chemotherapy, operative resection, postoperative chemotherapy, and radiation, had been documented as finished. Patients were considered to have received a blood transfusion if any blood product (packed red blood cells, plasma, platelets, etc.) had been administered *outside* of the operating room. Nearly every patient received some type of blood transfusion *in* the operating theatre and so these cases were not considered among the blood transfusion status variable.