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Original Article

Comparative Study Between Intra Operative Difficulties in the Management of Wilms' Tumor by SIOP and COG Protocol

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Abstract

Background: The survival of Wilms' tumor patients with favorable histology has improved dramatically in response to the introduction and use of current multimodal therapy. Though the SIOP and COG approaches produce nearly identical clinical outcomes, a valid debate about the relative merits of each approach continues.

Objective: To Compare the intra operative difficulties in management of Wilms' tumor by SIOP and COG protocol.

Methods: This cross-sectional observational study was carried out in the Department of Pediatric Surgery in Dhaka Medical College Hospital, Dhaka from January, 2021 to July, 2022 over a period of 19 months to compare the intra operative difficulties in the management of Wilms' tumor by SIOP and COG protocol. A total of 20 patients with Wilms' tumor scheduled for surgery at the Department of Pediatric Surgery, Dhaka Medical College Hospital, Dhaka and Bangladesh Shishu (Children) Hospital and Institute, Dhaka were enrolled in this study as per selection criteria. Two protocols were compared on the basis of per operative tumor spillage, complete resection, operative time, per operative blood loss, tumor weight and lymph node sampling. Statistical Package of Social Science (SPSS) 23 was used for data analysis.

Results: More than half of the children were ≤2.5 years old. Tumor spillage was observed significantly lower in SIOP group (10.0%) than in COG group (70.0%) in this study ($p<0.05$). Complete resection was found in all cases of SIOP and 70.0% cases of COG group ($p>0.05$). Regarding tumor stages, stage I and II were 40.0% each and stage III was 20.0% in SIOP group. In COG group, Stage I, stage II and stage III were 20.0%, 10.0% and 70.0% respectively ($p>0.05$). Lymph node sampling could be done in 80.0% cases in SIOP group and 50.0% cases in COG group ($p>0.05$). Median operative time was 80 min in SIOP group and 120 min in COG group but the difference was not statistically significant ($p>0.05$). Blood loss was smaller in SIOP group (median: 60 ml) than COG group (median: 65 ml), but the difference was not statistically significant ($p>0.05$). Tumor weight was lighter in SIOP group (median: 550gm) than COG group (median: 675gm) ($p>0.05$).

Conclusion: According to this study findings, SIOP protocol showed less operative difficulties than COG protocol in the management of Wilms' tumor.

Keywords: Wilms' tumor, pediatric oncology, intraoperative difficulties, Société Internationale d'Oncologie Pédiatrique (SIOP), Children's Oncology Group (COG), tumor management, surgical complications, nephrectomy, comparative study, pediatric surgery

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Introduction:

Wilms' tumor (WT) is the most common malignant renal neoplasm in children and ranks as the third most frequent pediatric malignancy [1]. It represents a major success story in pediatric oncology, with current multimodal treatment achieving cure rates approaching 90% [2]. The incidence of WT is approximately 1 per 10,000 children in Europe and North America, but notably lower in Asian countries. Although most studies report no gender difference, some Asian populations show a slightly higher prevalence among females [3].Pediatric renal tumors differ significantly from adult renal malignancies in their origin, biological behavior, and response to treatment. While adult renal cancers are predominantly carcinomas, childhood renal tumors like WT are embryonal in nature, characterized by rapid growth and favorable treatment outcomes [4]. First described by Thomas F. Rance in 1814 and later elaborated by Max Wilms in 1899[5], the tumor has since borne his name [4,5]. Though primarily renal, rare extrarenal sites such as the retroperitoneum, testis, uterus, and mediastinum have been documented[6]. WT arises from pluripotent embryonic renal precursor cells, making it an embryonic tumor. About 10% of cases are associated with congenital anomalies or genetic syndromes. The remarkable improvement in survival is attributed to multidisciplinary advances involving surgery, chemotherapy, and radiotherapy [7,8]. Two major collaborative groups—the Children's Oncology Group (COG) and the Société Internationale d'Oncologie Pédiatrique (SIOP)—have developed standardized treatment protocols achieving more than 90% five-year survival. The primary difference between these protocols lies in the timing of surgery: COG advocates upfront nephrectomy, whereas SIOP recommends preoperative chemotherapy [3]. Surgical excision remains central to management, requiring meticulous removal, accurate staging, and prevention of tumor spillage—events that can upstage disease and worsen prognosis [9]. Preoperative chemotherapy, as per SIOP, reduces tumor size, vascularity, and spillage risk by inducing fibrous pseudocapsule formation, facilitating safer excision [10]. Conversely, COG's upfront surgery approach may pose technical challenges in large tumors due to distorted anatomy and fragile capsules, increasing spillage risk [11]. Since tumor rupture elevates relapse rates and mandates intensified therapy with associated late effects, understanding intraoperative difficulties between both protocols is crucial. Hence, this study aims to compare the intraoperative challenges encountered in the management of Wilms' tumor following SIOP and COG guidelines.

Materials and Methods:

This cross-sectional observational study was conducted in the Department of Pediatric Surgery, Dhaka Medical College Hospital, Dhaka, in collaboration with Bangladesh Shishu (Children) Hospital & Institute, Dhaka, over a period of 19 months from January 2021 to July 2022. The study population included all patients diagnosed with Wilms' tumor who underwent surgery in the aforementioned institutions during the study period. A total of 20 patients were enrolled after fulfilling the inclusion and exclusion criteria, with 10 patients treated following the SIOP protocol (Group A) and 10 following the COG protocol (Group B).

Sample size was determined using the formula for comparing two proportions, considering 74.0% of inadequate lymph node sampling in the COG group[12] and 22.0% in the SIOP group (assumed), with $Z\alpha = 1.96$ and $Z\beta = 1.64$, resulting in an estimated sample size of 10 in each group. Patients were selected consecutively through purposive sampling. Children aged 6 months to 14 years with Stage I–III Wilms' tumor were included. Exclusion criteria comprised bilateral tumors, distant metastasis, recurrent tumors, Wilms' tumor in solitary or horseshoe kidney, syndromic cases (WAGR, Denys-Drash, Beckwith-Wiedemann syndromes), and lack of parental consent.

Informed written consent was obtained from parents or legal guardians after explaining the study's objectives, risks, and benefits. Ethical approval was granted by the Ethical Review Committees of both institutions. Detailed history, physical examination, and necessary investigations were performed preoperatively. In Group A (SIOP), patients received neoadjuvant chemotherapy prior to surgery, followed by postoperative chemotherapy/radiotherapy. In Group B (COG), primary surgery was performed first, followed by adjuvant therapy.

Intraoperative parameters including tumor spillage, completeness of resection, operative time, blood loss, tumor weight, and adequacy of lymph node sampling were documented. Data were recorded using a predesigned data collection sheet. Qualitative variables were presented as frequencies and percentages, while quantitative variables were expressed as medians with ranges. Statistical analyses were performed using SPSS version 23. The Mann-Whitney U test was used for continuous variables, Chi-square and Fisher's

Exact tests for categorical variables. A p-value <0.05 was considered statistically significant.

Results

A total of 20 patients with Wilms' tumorscheduled for surgery at the Department of Pediatric Surgery, Dhaka Medical College Hospital, Dhaka and Bangladesh Shishu(Children) Hospital and Institute, Dhaka were enrolled in this study according to selection criteria. Two protocols were compared on the basis of per operative tumor spillage, complete resection, operative time, per operative blood loss, tumor weight and lymph node sampling. The results were as follows:

Table 1: Demographic profile of the study subjects (N=20)

	Group-A (SIOP)	Group-B (COG)	p-value
Age (years)			
≤2.5	4 (40.0)	7 (70.0)	
>2.5	6 (60.0)	3 (30.0)	
Median (min-max)	3 (0.67- 8.58)	2.1 (0.5 – 5.0)	0.353
Gender			
Male	4 (40.0)	4 (40.0)	1.000
Female	6 (60.0)	6 (60.0)	

Mann-Whitney U test and Fisher's Exact test was done

Table 1 shows distribution of the study subjects according to age. Median age of the study subjects was 3.0 years and 2.1 years in SIOP and COG group respectively. Females were predominant than males in both the groups.

Table 2: Comparison of the study subjects according to tumor spillage (N=20)

	Group-A (SIOP)	Group-B (COG)	p-value
Absent	9 (90.0)	3 (30.0)	0.020
Occurred	1 (10.0)	7 (70.0)	

Fisher's Exact test was done.

Table 2 shows comparison of the study subjects according to tumor spillage. Spillage was observed significantly higher in COG group than SIOP group.

Table 3: Comparison of the study subjects according to resection (N=20)

Resection	Group-A (SIOP)	Group-B (COG)	p-value
Complete	10 (100.0)	7 (70.0)	0.211
Incomplete	0 (0.0)	3 (30.0)	

Fisher's Exact test was done.

Table 3 shows comparison of the study subjects according to resection. Complete resection was found in all cases of SIOP and 70.0% cases of COG group.

Table 4: Comparison of the study subjects according to stages of tumor (N=20)

Stages	Group-A (SIOP)	Group-B (COG)	
Stage I	4 (40.0)	2 (20.0)	
Stage II	4 (40.0)	1 (10.0)	
Stage III	2 (20.0)	7 (70.0)	

Chi-Square test was done.

Table 4 shows comparison of the study subjects according to stages of tumor. There was no significant difference in stages between the two groups. Tumor stage III was more in group B due to tumor spillage.

Table 5: Comparison of the study subjects according to lymph node sampling (N=20)

Lymph node sampling	Group-A (SIOP)	Group-B (COG)	p-value
Done	8 (80.0)	5 (50.0)	0.350
Not done	2 (20.0)	5 (50.0)	

Fisher's Exact test was done.

Table 5 shows comparison of the study subjects according to lymph node sampling.

Table 6: Comparison of operating time, blood loss and tumor weight (N=20)

	Group-A (SIOP) Median (Min-max)	Group-B (COG) Median (Min-max)	p-value
Operative time (min)	80 (60 - 240)	120 (60 - 180)	0.190
Blood loss (ml)	60 (25 - 220)	65 (30 - 500)	0.739
Tumor weight (gm)	550 (100-1200)	675 (150-1500)	0.393

Mann-Whitney U test was done.

Operating time was shorter in SIOP group than COG group, but the difference was not statistically significant. Blood loss was smaller in SIOP group than COG group but the difference was not statistically significant. Tumor weight was lighter in SIOP group than COG group, but the difference was not statistically significant.

Discussion

Both the SIOP and COG protocols have advantages and disadvantages. According to COG investigators, the SIOP protocol results in unnecessary chemotherapy in benign / low grade tumors / cases with other diagnoses than Wilms' tumor; changes in tumor histology; and loss of exact staging information. SIOP researchers clarify that because anaplasia is not responsive to chemotherapy, risk stratification remains unchanged. Furthermore, postoperative chemotherapy and radiotherapy doses can be tailored to the remnant tumor. According to the SIOP investigators, neoadjuvant chemotherapy has the advantage of reducing tumor size as well as tumor spillage, allowing for simply minimally invasive surgery with better outcomes and even the possibility of renal sparing surgery in selected cases based on post-chemotherapy tumor size reduction. COG has an advantage over SIOP in that it preserves the molecular biology of the untreated tumor, which is of greater research value. According to the investigators, another advantage of the COG protocol is that it avoids unnecessary chemotherapy in low grade cases as well as cases with histological diagnoses other than Wilms' tumor. SIOP investigators argue that it worsens the prognosis of high-grade cases, of which there are a disproportionately large number, for the need of neoadjuvant chemotherapy. The benefits of SIOP outweigh the risks and are especially important in the Indian subcontinent, where a significant proportion of patients present in advanced stages.[13] In this study, the median age of the study subjects was 3.0 years and 2.1 years in SIOP and COG group respectively. More than half of the children were ≤2.5 years old. In the study of Hasina et al[8] most of the children with Wilms' tumor were 2 to 4 years old. Elgendy et al[12] studied 37 patients with Wilms' tumors who were treated following COG protocol. Their median age was 3.1 years, and 54.1% of them were below 3 years. The peak age of incidence is approximately 3–4 years [8]. Tumor spillage was observed significantly lower in SIOP group (10.0%) than in COG group (70.0%) in this study. Intra-operative spillage was 9.7% in the study of Gow et al[11] where COG protocol was followed. Intra-operative tumor rupture and spillage was 18.52% in the study of Elgendy et al [12] where COG protocol was followed.In a study using the COG procedure, 22.2% of children experienced intraoperative tumor spillage [14]. In a research where the SIOP procedure was followed, only 3.3% of children experienced intraoperative tumor spillage [15].In this study, complete resection was found in all cases of SIOP and 70.0% cases of COG group. There was no significant difference in resection between the two procedures. In COG group complete resection could not done in two patients due to excess blood loss and huge adherence to surrounding structures and in another patient tumor is hugely large in size. There was no significant difference in resection between the two procedure.Regarding tumor stages, stage I and II were 40.0% each and stage III was 20.0% in SIOP group. In COG group, Stage I, stage II and stage III were 20.0%, 10.0% and 70.0% respectively. There was no significant difference in stages between the two groups. In one study among the patients, 12 (32.4%), 11 (29.7%), 10 (27%), and 4 (10.8%) belonged to stages I, II, III, and IV, respectively [12].In this study lymph node sampling could be done in 80.0% cases in SIOP group and 50.0% cases in COG group. But there was no significant difference in lymph node sampling between the two groups. Failure of lymph nodes documentation was 74.07% in the study of Elgendy et al [12] where COG protocol was followed.Median operative time was 80 min in SIOP group and 120 min in COG group but the difference was not statistically significant ($p>0.05$). Blood loss was smaller in SIOP group (median: 60 ml) than COG group (median: 65 ml), but the difference was not statistically significant ($p>0.05$). Tumor weight was lighter in SIOP group (Median: 550gm) than COG group (median: 675gm), but the difference was not statistically significant.In terms of the surgical challenge of nephrectomy, the non-ruptured group's median operation time and per operative blood loss were 250 minutes and 8.8 ml/kg body weight, respectively in a procedure followed by COG protocol. In contrast, the ruptured group's median operation duration and per operative blood loss were 491 minutes and 91.3 ml/kg of body weight, respectively [14].When compared to the COG protocol in this study, spillage was observed to be considerably lower in the SIOP group ($p<0.05$). In comparison to COG, SIOP performed more complete resections and lymph node sampling ($p >0.05$). In comparison to the COG protocol, the SIOP procedure took less time, lost less blood, and had smaller tumors ($p>0.05$). In this study, the SIOP protocol produced better overall results than the COG approach.

Conclusion

Among the outcome variable of this study, Tumor spillage was observed to be significantly lower in the SIOP group comparing to COG group. In comparison to COG, SIOP performed more complete resections and lymph node sampling, took less operative time, had less per operative blood loss and less tumor weight tumors in comparison to COG procedure. Therefore,In this study, the SIOP protocol produced better overall results than the COG approach.

Limitation

There are some limitations of this study. These are as follows:

- Nephrectomies were performed by multiple surgeons. The rate of spillage by the individual surgeon was not mentioned in this study.
- The samples were taken purposively, so there might be a chance of bias which could influence the results.

Recommendations

It is recommended that:

- Parents should seek early medical service in cases of any abdominal lump.
- Primary care physicians and general practitioners should remain alert about the children presenting with abdominal mass and refer them to a specialized center forproper management.

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