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Editorial

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The Evolving Role of Surgical Oncology in the Era of Precision Medicine and Immunotherapy

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Abstract

Surgical oncology used to be the main way to cure solid tumors, but things are changing with precision medicine and immunotherapy. New tools like genomic profiling and immune checkpoint inhibitors allow doctors to shrink or even remove tumors using medicines, reducing the need for surgery in some cases. This has started debates about when surgery is really needed, and in some cancers, organ-preserving or "watch and wait" approaches are being tried.

Today, surgical oncologists work closely with molecular tumor boards, use genomic and immunologic knowledge, and follow more personalized treatment plans. Training now includes genomics, immunology, and research skills in addition to surgery. Still, there are big global gaps—wealthy countries move toward personalized care, while low-resource settings still depend mostly on surgery.

The modern aim is not just cure, but also preserving organs, protecting quality of life, and ensuring dignity. By embracing teamwork and innovation, surgical oncology continues to play a key role in cancer care.

Surgical oncology has long stood as the cornerstone of cancer care. For decades, the sequence was simple: surgery first, then chemotherapy or radiotherapy when needed. But in today's era of precision medicine and immunotherapy, this order is no longer fixed. Advances in genomics and immune-based treatments mean systemic therapy can precede, complement, or even replace surgery. As cancer treatment becomes more personalized, surgical oncology must evolve to remain central in multidisciplinary care.

From Scalpel to Systems

Traditionally, surgery was the best chance for cure in solid tumors. Chemotherapy and radiotherapy were supportive, often used after resection. Now, genomic profiling allows us to identify mutations responsive to targeted drugs such as EGFR inhibitors in lung cancer or BRAF inhibitors in melanoma[1]. Likewise, immune checkpoint inhibitors such as PD-1 and CTLA-4 blockers have transformed survival outcomes in diseases once considered intractable[2].

These advances have changed surgical decision-making. Patients who once needed extensive resections may now experience dramatic tumor shrinkage after systemic therapy. In some trials, neoadjuvant immunotherapy has led to complete responses, raising the question of whether traditional surgical margins-or even surgery itself-are always required[3].

Timing and Scope of Surgery

One of the biggest debates today concerns the timing and extent of surgery. Should all patients still undergo

surgery after systemic therapy, or can exceptional responders avoid it? Can radical resections be replaced by organ-preserving approaches guided by treatment response?

For instance, in rectal cancer, total neoadjuvant therapy has enabled some patients to follow a "watch and wait" strategy, avoiding surgery entirely under strict monitoring[4]. This represents a shift not only in survival outcomes but also in preserving quality of life.

Surgery in a Molecular Ecosystem

Surgical oncologists now practice in an environment where molecular tumor boards, biomarker analyses, and genomic sequencing are routine[5]. Surgery is no longer an isolated technical act but part of a continuum of personalized, system-guided care. This requires surgeons to understand genomic data, tumor immunology, and evolving drug landscapes.

The modern role demands humility and collaboration. Surgical oncologists must work closely with medical oncologists, pathologists, radiologists, and basic scientists. Decisions are rarely binary. Instead, they reflect the interplay between systemic response, tumor biology, and patient values.

Global Disparities

While precision medicine and immunotherapy are advancing rapidly, their benefits are unevenly distributed. In high-income countries, genomic sequencing and immune-based therapies are increasingly routine. In many low-resource settings, however, surgery remains the primary modality due to late presentations and limited access to systemic treatments[6].

This creates a two-tier system: organ-preserving, molecularly tailored care in wealthier regions versus radical, life-altering surgery in resource-limited countries. Bridging this gap requires investment in affordable diagnostics, infrastructure, and international training collaborations.

Training the Next Generation

Surgical training also needs to evolve. Traditional emphasis on anatomy and operative skill remains vital, but the next generation of surgical oncologists must also be literate in genomics, immunology, and clinical trial design[7].

Exposure to tumor boards, translational research, and simulation-based decision-making can prepare young surgeons for this integrated role. Without such adaptation, surgical oncology risks being sidelined in the precision era.

Organ Preservation and Functional Outcomes

Perhaps the most exciting promise of combining surgery with precision therapy is the shift toward organ preservation. Breast-conserving surgery has been a long-standing goal, but systemic therapies now make it possible in cases that once required mastectomy[8]. Similarly, in lung cancer, neoadjuvant immunotherapy is enabling less extensive resections[9].

The philosophy is changing: the aim is not only to cure cancer but also to preserve organs, function, and quality of life. Surgeons are becoming architects of care that balances eradication of disease with preservation of dignity and survivorship.

Collaboration as Standard

The future of surgical oncology lies in collaboration. Tumor boards should not be optional but standard practice. The surgeon's role is no longer just technical execution but providing judgment that integrates anatomy, biology, systemic response, and patient preference.

By embracing this collaborative and adaptive role, surgical oncologists can remain indispensable in modern cancer care.

Surgical oncology stands at a turning point. Precision medicine and immunotherapy are not threats but opportunities to reimagine our discipline. The scalpel still matters—but it must work in harmony with the tools of molecular biology and immune science.

By adapting training, embracing genomic data, fostering collaboration, and addressing global disparities, surgical oncologists can remain central to the evolving story of cancer care.

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Original Article

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Weekly Cisplatin Vs. Three-weekly Cisplatin in Concurrent Chemoradiotherapy of Locally Advanced Head and Neck Squamous Cell Carcinoma- Evaluation of Short-Term Response and Toxicity

Taohida Yasmin[1], Kazi Manzur Kader[2], Muhammad Masudul Hassan Arup[3], Md. Johirul Islam[4], Sadia Afroz[5], Afroza Akhter[6], Tania Sultana[7]

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Abstract

Background: *Head and neck squamous cell carcinoma (HNSCC) is the fifth most common cancer globally and highly prevalent in Bangladesh, where most patients present at a locally advanced stage. Concurrent chemoradiotherapy (CCRT) with cisplatin is the standard of care, but the optimal dosing schedule remains debated. This study compares the short-term efficacy and toxicity of weekly versus three-weekly cisplatin-based CCRT.* ***Methods:*** *A quasi-experimental study was conducted at the National Institute of Cancer Research and Hospital, Dhaka, from June 2015 to July 2016. Sixty patients with locally advanced HNSCC were non-randomly assigned to receive either weekly cisplatin (40 mg/m²) or three-weekly cisplatin (100 mg/m²) concurrent with radiotherapy (66–70 Gy). Response and toxicities were assessed using RECIST 1.0 and RTOG/CTCAE criteria.* ***Results:*** *The baseline characteristics were similar between arms. Complete response rates were comparable: 68% in the weekly group vs. 72.4% in the three-weekly group ($p > 0.05$). Acute toxicities—including mucositis, hematologic, and gastrointestinal effects—were lower in the three-weekly group, although not statistically significant. No difference in renal toxicity was observed. Both regimens were well-tolerated.* ***Conclusion:*** *Weekly cisplatin-based concurrent chemoradiotherapy showed comparable short-term tumor response to the standard three-weekly regimen, with acceptable and comparable acute toxicity. Given its favorable tolerability, ease of administration, and suitability for outpatient care, weekly cisplatin may be considered a practical and patient-friendly alternative in low-resource settings where intensive monitoring is not feasible.*

Keywords*: Head and neck cancer, concurrent chemoradiotherapy, cisplatin, weekly dosing, short-term response*

Introduction

Head and neck squamous cell carcinoma (HNSCC) refers to malignancies arising from the mucosal surfaces of the upper aerodigestive tract. It is the fifth most common cancer globally, with an estimated 550,000 new cases annually. [1–3] In Bangladesh, hospital-based registry data from the National Institute of Cancer Research & Hospital (NICRH) report a mean patient age of 50 years and show that lip/oral cavity/pharyngeal cancers constitute 11.1% of all cancers recorded.[4] Earlier, another hospital based registry data indicated that approximately two-thirds (~66%) of cancer patients are aged 30–65 years, supporting the predominance of middle-aged presentations.[5]

Tobacco use (smoking and smokeless), alcohol, and viral infections such as HPV and EBV are key risk factors, with regional variations influenced by lifestyle and socioeconomic factors. In South Asia, betel quid chewing and poor nutrition are additional contributors.[6]

HNSCC is clinically categorized into early-stage (Stage I–II), locoregionally advanced (Stage III–IVB), and metastatic (Stage IVC) disease.

Treatment depends on the stage. Definitive local therapy (surgery and/or radiotherapy) is central to managing locoregionally advanced HNSCC, though it carries a high risk of recurrence and substantial morbidity (e.g., swallowing difficulty, speech impairment). To enhance local control and survival while preserving organ function, chemotherapy has been incorporated into treatment strategies, including operable cases.[7]

Concurrent chemoradiotherapy (CCRT) has emerged as a standard approach for its radiosensitizing benefits. Cisplatin, in particular, enhances radiation effects by interfering with sublethal damage repair and synchronizing tumor cells to prevent resistant clone emergence.[8] Therefore, the addition of chemotherapy to radiotherapy improves local control and survival. Among the various agents, cisplatin offers the most consistent survival benefit, with meta-analyses showing an 8% increase in overall survival over radiotherapy alone.[9] The standard regimen—100 mg/m² cisplatin every three weeks during radiotherapy—is effective but often poorly tolerated due to significant toxicities.

As a result, weekly cisplatin regimens (40 mg/m²) are increasingly explored, aiming to reduce acute toxicity while maintaining efficacy. Smaller, more frequent doses may provide consistent radiosensitization with better tolerability, especially in resource-limited settings and nutritionally compromised populations.

Head and neck squamous cell carcinoma (HNSCC) is a major public health concern in Bangladesh and a substantial proportion of patients present with locoregionally advanced disease, consistent with local hospital-based series in which about half of oral cancer patients present at stage III–IV.[6] This mirrors global patterns where most HNSCC cases are diagnosed at locally advanced stages.[7] Standard concurrent chemoradiotherapy (CCRT) with three-weekly high-dose cisplatin (100 mg/m²) is associated with improved survival but also significant acute toxicities. In resource-constrained settings, where malnutrition and limited access to supportive care are common, this regimen is often poorly tolerated.

Weekly cisplatin regimens have emerged as a promising alternative, potentially offering comparable efficacy with improved tolerability. However, data from South Asian populations—particularly those reflecting real-world constraints—remain limited. This study aims to evaluate the short-term treatment response and toxicity profiles of weekly cisplatin versus three-weekly cisplatin when used concurrently with radiotherapy in locally advanced HNSCC.

Methodology

This quasi-experimental study, conducted at NICRH, Dhaka, from June 2015 to July 2016, aimed to compare the therapeutic efficacy and toxicity of weekly versus three-weekly cisplatin given concurrently with radiotherapy in patients with locally advanced Head and Neck Squamous Cell Carcinoma. Sixty eligible patients, diagnosed with Stage III-IVB HNSCC of various subsites and meeting specific inclusion criteria (age ≤70, KPS ≥70, no prior treatment or distant metastasis), were allocated into two groups: Arm A received weekly cisplatin (40 mg/m² for six cycles) and Arm B received three-weekly cisplatin (100 mg/m² on days 1, 22, and 43). Ethical approval and informed consent were obtained. The primary objectives were to compare short-term tumor response rates and treatment-related toxicities (skin, mucosal, hematologic, renal), and to analyze factors influencing outcomes. Ultimately, 28 patients from Arm A and 29 from Arm B were included in the final analysis.

Patients received 66-70 Gy of radiation over 7 weeks. The majority (93%) were treated with 2D cobalt-60, with the remainder receiving 3D-CRT. Pre-treatment, all

patients underwent comprehensive evaluation including imaging and blood tests. During treatment, patients had weekly assessments for toxicity and blood counts. Post-treatment follow-up continued for 6 months, with response assessed at 12 weeks using RECIST 1.0. Toxicities were graded weekly using RTOG and CTCAE v4.0 criteria. Supportive care included antiemetics, hydration for cisplatin, pain management, nutritional support, and management of hematologic/renal issues. Smoking cessation counselling was also provided. Treatment modifications were made for significant toxicities. Statistical analysis involved SPSS v22, using t-tests for continuous variables and Chi-square or Fisher's Exact tests for categorical variables, with $p<0.05$ considered significant.

Result

At the end of the study, we had a total of 57 patients' data available to be interpreted, 28 patient in Arm A and 29 patients in Arm B for the final results analysis. Baseline characteristics—including age, sex, occupation, socioeconomic status, education, performance status, smoking/tobacco/betel-quid use, and tumor stage—were comparable between arms (all $p > 0.05$). The most frequent primary subsites were the larynx and oral cavity, with no significant differences in distribution between groups ($\chi^2=0.86$, $p=0.93$; Figure 1). Baseline Karnofsky Performance Status (KPS) distributions were also similar comparable (Fisher's exact $p = 0.764$; Figure 2) Presenting features were dominated by neck-node swelling, followed by pain, dysphagia, and weight loss; rarer symptoms included otalgia and ear stuffiness (Figure 3).

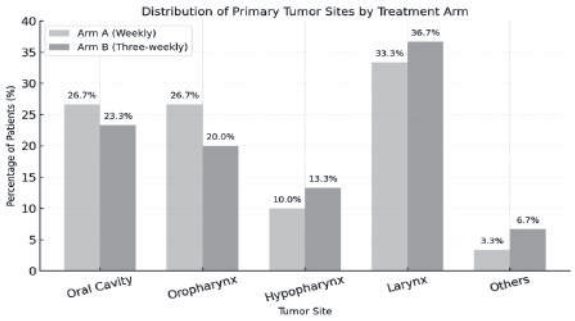


Figure 1. *Distribution of primary tumor sites among patients receiving weekly (Arm A) and three-weekly (Arm B) cisplatin-based concurrent chemo-radiotherapy. The most common subsites were the larynx and oral cavity in both arms, with no significant differences in distribution between groups.*

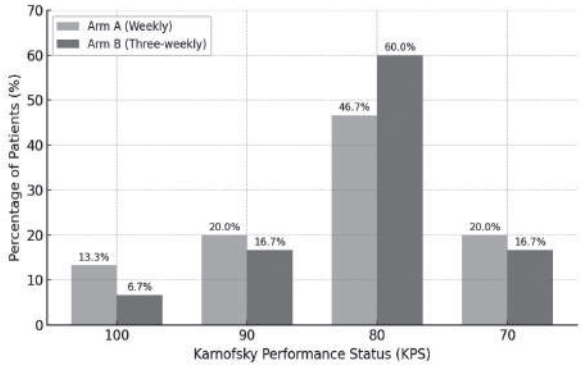


Figure 2. *Distribution of Karnofsky Performance Status at baseline in Arm A (weekly cisplatin) and Arm B (three-weekly cisplatin). The distributions were comparable between groups (Fisher's exact p = 0.764).*

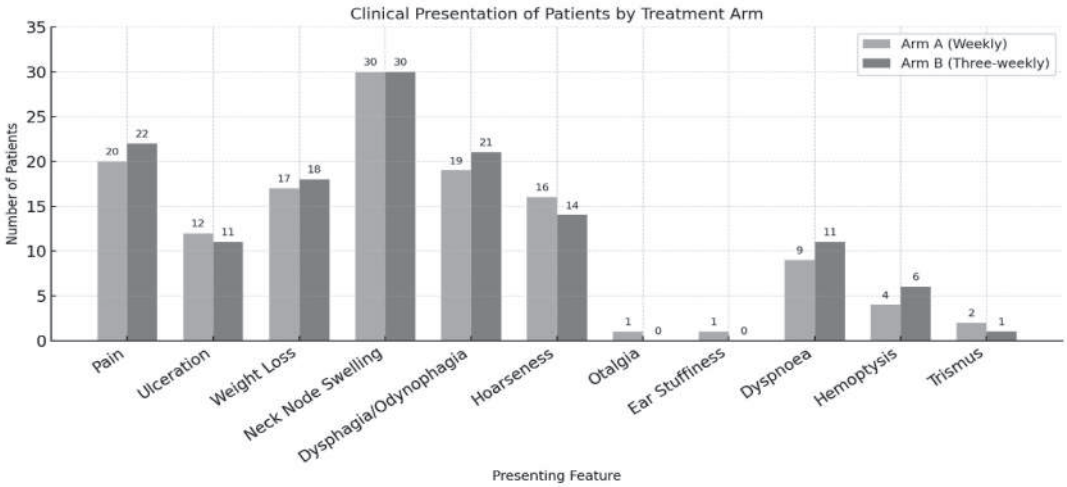


Figure 3. *Distribution of clinical presenting features among patients in Arm A (weekly cisplatin) and Arm B (three-weekly cisplatin). Neck node swelling was the most common feature across both groups, followed by pain, dysphagia, and weight loss. Rare symptoms such as otalgia and ear stuffiness.*

Table 1: Incidence of Treatment-Related Toxicities by Regimen and Time Point

Toxicity	Week	Grade	Weekly Cisplatin (n=28)	Three-Weekly Cisplatin (n=29)	*p*-value
Oral Mucositis	1	0	28 (100)	29 (100)	-
	3	0	14 (50)	16 (55.2)	.091
		1	13 (46.4)	12 (41.4)	
		2	1 (3.6)	1 (3.4)	
	6	1	14 (50)	15 (51.7)	.287
		2	8 (28.6)	10 (34.5)	
		3	6 (21.4)	4 (13.8)	
Skin Toxicity	1	0	28 (100)	29 (100)	-
	3	1	13 (46.4)	14 (48.3)	.214
		2	15 (53.6)	15 (51.7)	
	6	1	9 (32.1)	11 (37.9)	.588
		2	11 (39.3)	11 (37.9)	
		3	8 (28.6)	7 (24.1)	
Hematologic Toxicity	1	0	28 (100)	29 (100)	-
	3	0	20 (71.4)	21 (72.4)	.547
		1	4 (14.3)	5 (17.2)	
		2	4 (14.3)	3 (10.3)	
	6	0	18 (64.3)	19 (65.5)	.559
		1	5 (17.9)	6 (20.7)	
		2	5 (17.9)	4 (13.8)	
Nausea	1	0	28 (100)	29 (100)	-
	3	0	8 (28.6)	10 (34.5)	.254
		1	20 (71.4)	19 (65.5)	
		2	1 (3.6)	0 (0)	
	6	1	18 (64.3)	20 (69.0)	.988
		2	10 (35.7)	9 (31.0)	
Vomiting	1	0	28 (100)	29 (100)	-
	3	0	8 (28.6)	10 (34.5)	.978
		1	20 (71.4)	19 (65.5)	
	6	0	6 (21.4)	6 (20.7)	1.00
		1	14 (50)	16 (55.2)	
		2	8 (28.6)	7 (24.1)	
Renal Toxicity	1	0	28 (100)	29 (100)	-
	3	0	26 (92.9)	28 (96.6)	.784
		1	2 (7.1)	1 (3.4)	
	6	0	22 (78.6)	24 (82.8)	.622
		1	6 (21.4)	5 (17.2)	

Abbreviation: *n*, number of patients.

Data are presented as n (%).

p-value are for the comparison of the distribution of toxicity grades between the two arms at each time point (Fisher's exact test).

Treatment-related toxicities (Table 1) were minimal at Week 1 in both arms. For oral mucositis, Week-3 grade distributions were similar (Grade 0/1/2: 50.0/46.4/3.6% in Arm A vs 55.2/41.4/3.4% in Arm B; p=0.091). By Week 6, Grade ≥2 mucositis occurred in 50.0% (Arm A) and 48.3% (Arm B), with comparable grade composition (Grade 1/2/3: 50.0/28.6/21.4% vs 51.7/34.5/13.8%; *p*=0.287. Skin toxicity showed a parallel trajectory: Grade ≥2 at Week 3 was 53.6% (Arm A) vs 51.7% (Arm B; *p*=0.214), rising by Week 6 to 67.9% vs 62.0% with similar grade mix (*p*=0.588). Gastrointestinal symptoms were uncommon early; at Week 3, Grade ≥2 nausea was 3.6% vs 0% (*p*=0.254), and by Week 6 it increased comparably to 35.7% vs 31.0% (*p*=0.988). Grade ≥2 vomiting was 0% at Weeks 1 and 3 and rose modestly by Week 6 to 28.6% vs 24.1% (*p*=1.00). Renal events were mild overall; no Grade ≥2 toxicities occurred. Grade ≥1 increased from 0% at Week 1 to 7.1% vs 3.4% at Week 3 (*p*=0.784) and 21.4% vs 17.2% at Week 6 (*p*=0.622). Hematologic toxicity remained low: Grade ≥2 was 14.3% vs 10.3% at Week 3 (*p*=0.547) and 17.9% vs 13.8% at Week 6 (*p*=0.559). Overall, toxicity increased overtime as expected during CCRT, but between-arm differences were not statistically significant at the assessed time points.

Across follow-up at 6, 12, and 18 weeks, anorexia tended to persist slightly more often in Arm B (e.g., 63.3% vs 76.7% at 6 weeks; 46.7% vs 56.7% at 18 weeks), while dysphagia and pain declined at similar rates, with transiently higher pain in Arm B at 12 weeks; Weight loss remained minimal and similar between arms throughout follow-up (Figure 4).

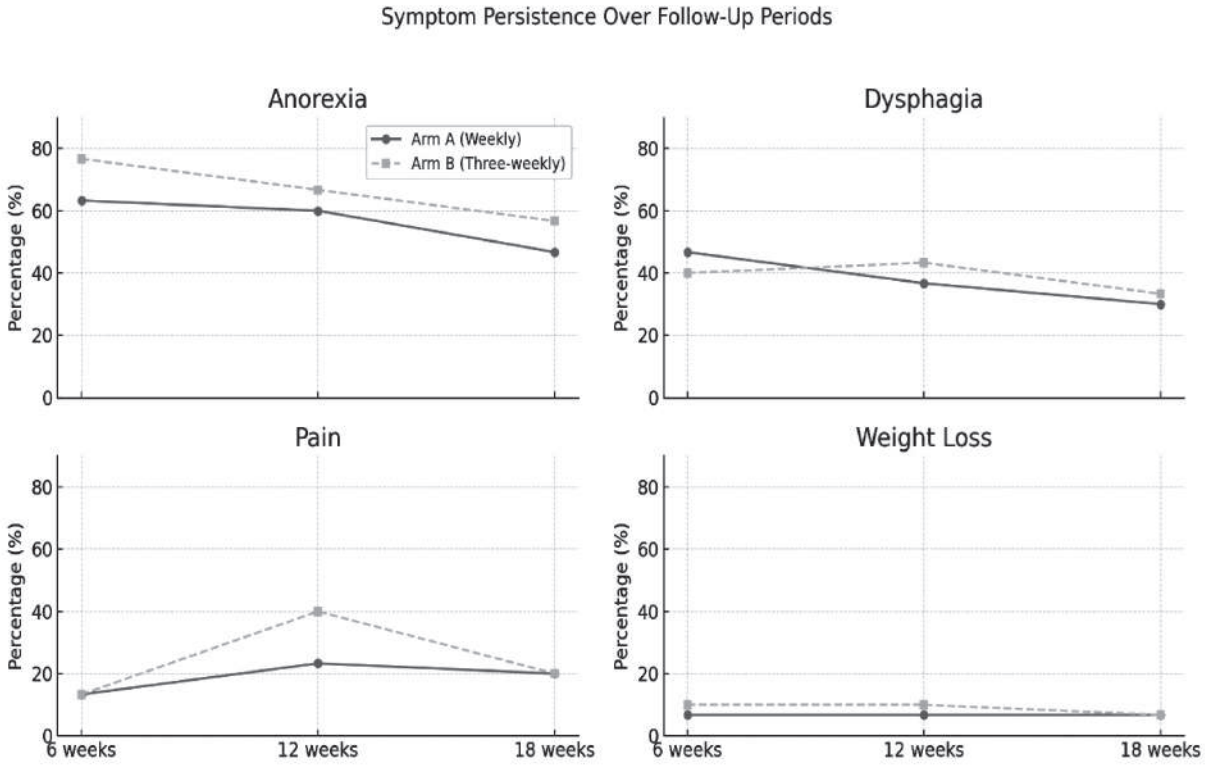


Figure 4. *Symptom persistence over 6-, 12-, and 18-weeks post-treatment in patients receiving weekly (Arm A) and three-weekly (Arm B) cisplatin. Anorexia remained more prevalent in Arm B throughout follow-up. Dysphagia and pain were comparable but showed a slower resolution in Arm B. Weight loss remained minimal and similar in both arms. Pain was higher in Arm B at 12 weeks, was managed symptomatically.*

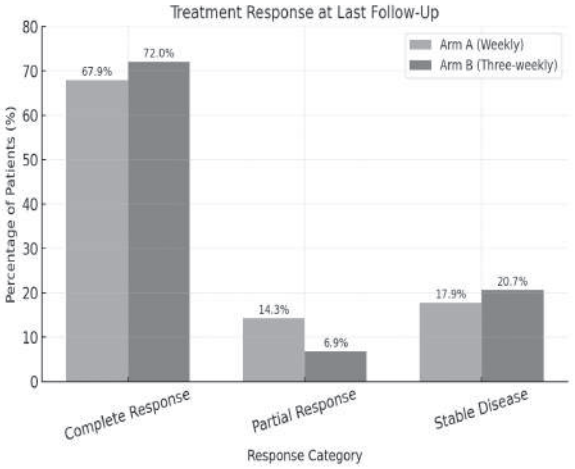


Figure 5. *Comparison of treatment response at last follow-up between Arm A (weekly cisplatin) and Arm B (three-weekly cisplatin). Complete response rates were slightly higher in Arm B (72%) than in Arm A (67.86%), though the difference was not statistically significant (p = 0.112). No cases of progressive disease were observed in either group*

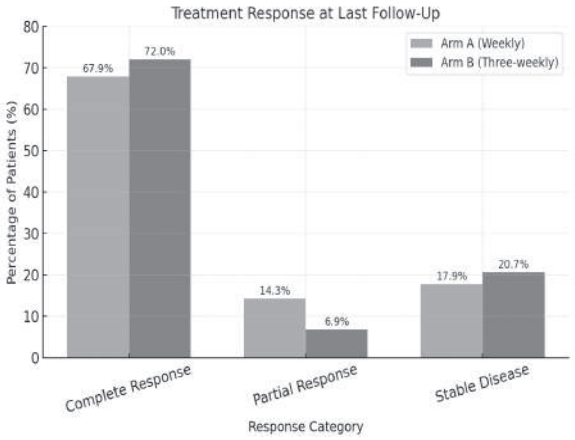


Figure 6. *Complete response (CR) by baseline Karnofsky Performance Status (KPS) showing CR rates were broadly similar across KPS strata in Arm A vs Arm B. pooled across arms. CR increased monotonically with higher KPS—50.0% at KPS 70 (5/10), 70.0% at KPS 80 (21/30), 81.8% at KPS 90 (9/11), and 83.3% at KPS 100 (5/6)—while between-arm differences within each KPS stratum were small.*

At 6-month post-treatment, the last follow-up, complete response (CR) were found in 67.9% of Arm A and 72.0% of Arm B, with partial response in 14.3% vs 6.9% and stable disease in 17.9% vs 20.7%; no progressive disease was observed. The difference in overall response was not statistically significant (p=0.112; Figure 5). When CR was examined against baseline KPS pooled across arms, CR increased with higher KPS—50.0% (KPS 70), 70.0% (KPS 80), 81.8% (KPS 90), 83.3% (KPS 100)—with borderline evidence of a positive trend (Cochran–Armitage Z=1.64; one-sided p=0.050, two-sided p=0.10), and small between-arm differences within each KPS stratum (Figure 6).

Discussion

Head and neck squamous cell carcinoma (HNSCC) is a common malignancy in Bangladesh, with the majority of patients presenting at a locally advanced stage. While concurrent chemoradiotherapy (CCRT) using high-dose three-weekly cisplatin (100 mg/m²) remains the standard of care globally, its high toxicity burden poses challenges in patient populations with poor nutritional status, limited supportive care access, and high treatment dropout risk.

In this study, we compared the efficacy and acute toxicity of weekly versus three-weekly cisplatin-based CCRT. At last follow-up, complete response was 67.9% in the weekly arm (19/28) and 72.4% in the three-weekly arm (21/29); the difference was not statistically significant (p=0.112). Our findings are consistent with prior research findings. the meta-analysis by Mohamed et al., which reported no significant differences between weekly and three-weekly cisplatin schedules in locoregional control (58% [95% CI, 53–63] vs 61% [56–65]; p=0.70), 2-year overall survival (74% [66–80] vs 67% [64–69]; p=0.67), 2-year progression-free survival (69% [59–77] vs 62% [58–65]; p=0.90), or grade 3–5 toxicities (36% vs 40%; p=0.37), supporting comparable efficacy and safety between regimen.[10]

Toxicity profiles in our cohort followed expected time courses during CCRT—rising from Week 1 to Week 6—but between-arm differences were small and not statistically significant at the assessed time points for mucositis, skin reactions, hematologic events, and gastrointestinal symptoms. This pattern aligns with earlier series that reported acceptable tolerability with weekly cisplatin in real-world settings, including reports emphasizing better mucosal tolerance or manageable hematologic toxicity with weekly schedules.[11-13] Although our data did not demonstrate significant separation by arm, the observed trends and the

cumulative clinical experience in resource-limited contexts support the notion that weekly dosing can be easier to deliver and monitor, potentially translating into steadier treatment continuity. Toxicities in our cohort rose over time but did not differ significantly between arms, which is consistent with several reports. Gupta et al**.** observed that weekly cisplatin with radical RT had moderate efficacy with acceptable acute toxicity, supporting feasibility in routine practice.[14] Kose et al. reported comparable efficacy to the three-weekly schedule with manageable toxicity for weekly cisplatin in concurrent CRT.[12] In a comparative cohort, Fayette et al. found the three-weekly 100 mg/m² regimen more toxic overall—showing more grade 3–4 mucositis/dermatitis, greater weight loss, more hospitalizations and RT interruptions—whereas the weekly schedule had better treatment completion.[13] A broader synthesis by Mohamed et al. showed no significant differences between weekly and three-weekly cisplatin for locoregional control (≈58% vs 61%), 2-year OS (≈74% vs 67%), 2-year PFS (≈69% vs 62%), or grade 3–5 toxicity (≈36% vs 40%), supporting comparable efficacy and safety across dosing schedules.[10] Jacinto et al. similarly emphasized better mucosal tolerance with weekly administration in regional experience.[11]

By contrast, Noronha et al**.** reported superior long-term locoregional control with phase 3 open-label non-inferiority study with the three-weekly 100 mg/m² regimen versus weekly 30 mg/m². Specifically, the 5-year locoregional control rates were 56.76% for the three-weekly arm versus 48.09% for the weekly arm. However, no significant difference in 5-year overall survival was observed between the two groups (50.55% vs. 43.60%; p = 0.19). while overall survival did not differ and ototoxicity was higher with high-dose cisplatin. These findings suggest that while the three-weekly cisplatin regimen takes the lead as standard regimen for better locoregional control, but it may be associated with increased ototoxicity, necessitating careful patient selection and monitoring.

From a clinical practice standpoint, with the limited availability of inpatient beds, inadequate staffing for close monitoring, patient with poor nutritional status, KPS and financial constraints among patients often hinder the safe administration of high-dose (100 mg/m²) cisplatin. Additionally, the need for rigorous hydration protocols and supportive care for managing acute toxicity, including nephrotoxicity and ototoxicity, is often unmet due to infrastructure limitations. As such, weekly cisplatin (30–40 mg/m²) remains a more practical, logistically simpler and better-tolerated option for concurrent chemoradiotherapy in the local context, ensuring continuity of care while minimizing treatment interruptions and hospitalization. This regimen can be administered in outpatient or even in ambulatory settings and may reduce treatment interruptions due to toxicity-related hospitalizations.

Conclusion

In this study, weekly cisplatin–based CCRT achieved short-term efficacy comparable to the standard three-weekly regimen, with no statistically meaningful differences in early locoregional control, short-term survival, or acute toxicity. Given its operational advantages—simpler hydration/monitoring and suitability for outpatient delivery—weekly cisplatin is a clinically reasonable alternative where resources and supportive care are constrained, and where treatment continuity is a priority.

These findings support the feasibility of adopting a weekly schedule in limited-resource settings to help maintain adherence and reduce unplanned admissions. However, our follow-up was limited to approximately six months; long-term outcomes (durable LRC, survival, late toxicities) were not assessed, and the study was modest in size. Larger studies with longer follow-up and contemporary RT techniques are warranted to define when the pragmatic benefits of weekly dosing offset potential long-term control advantages reported with three-weekly cisplatin

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Original Article

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Demographic and Clinical Profile of Paediatric Nasopharyngeal Carcinoma -Experience from National Institute of Cancer Research and Hospital, Bangladesh

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Abstract

Background: *Nasopharyngeal carcinoma (NPC) accounts for 35–50% of all nasopharyngeal malignancies in children. An increased incidence is usually observed in children aged 15 to 19 years. The majority of paediatric NPC cases present with advanced disease stage and undifferentiated histology. Even so, children have a better chance of survival. The National Institute of Cancer Research & Hospital (NICRH), Bangladesh, is unique in its ability to provide combined modality therapy. No previous study has been conducted at our center to assess the demographic and clinical profile of paediatric NPC cases.* ***Methods:*** *This cross-sectional study was conducted on children diagnosed with nasopharyngeal carcinoma between July 2016 and June 2022 to evaluate their clinical and demographic profiles. Information on age, sex, area of residence, month of enrollment, clinical presentation and duration, tumor staging and histopathological grading, and immunohistochemistry (IHC) reports was collected using a pre-structured data sheet with consent from guardians. Data were edited and analyzed using SPSS version 23.* ***Results:*** *A total of 62 children were included. Their ages ranged from 7.5 to 17 years, with a mean of 12.93 ± 2.56 years. Males were predominant, with a male-to-female ratio of 1.8:1. The majority (71.0%) of NPC cases occurred in children under 15 years. Regarding residence, 40.3% were from the northernmost districts, 21.0% from the southernmost districts, and 38.7% from various other regions. Cases occurred throughout the year, with peaks in March–April and November–December (each 19.4%). The most common clinical presentation was neck swelling (93.5%), followed by epistaxis (48.4%), nasal blockage (27.4%), and earache (12.9%). The duration of symptoms ranged from 1 to 12 months, with a mean of 4.75 ± 2.87 months. Advanced-stage disease (stages III, IVA, and IVB) was found in 83.9% of children. According to the WHO pathological grading system, 96.8% were type III (undifferentiated carcinoma). IHC showed EBV-associated LMP1 positivity in 90% (48/53) of tested cases.* ***Conclusion:*** *Most of the children with NPC were under 15 years of age and predominantly male. A notable cluster of cases originated from the northernmost parts of the country. Most patients presented with advanced-stage disease and undifferentiated histology.*

Keywords: *Paediatric, Nasopharyngeal carcinoma, Clinical, Demographic, profile, Bangladesh*

Introduction

Nasopharyngeal carcinoma (NPC) is a neoplasm arising from epithelial cells of the nasopharynx which account for about one-third of all cancers of the upper airways in children[1,2]. It is very rare in children younger than 10 years. In children aged 10-14 years incidence is 0.5 cases per 1 million per year whereas incidence increases to 1.3 cases per million per year in children aged 15 to 19 years[3]. Incidence varies with age, geographic factors, and ethnic factors, indicating that both genetic and environmental factors contribute to tumor development. NPC is endemic in South-east Asia like Southern China, Taiwan, Hong Kong; North Africa, and the Mediterranean basin[3-5]. The World Health Organization (WHO) recognizes three histological subtypes[6], among them children with nasopharyngeal carcinoma are more likely to have WHO type II or type III disease[4,5].

Common clinical presentation of nasopharyngeal carcinoma includes unilateral or bilateral neck swelling, nasal congestion and obstruction, epistaxis, headache, earache, otitis media etc. Cranial nerve palsy or trismus are other rare findings due to upward extension of the tumor leading to skull base erosion[2,7]. Same population-based studies reported that patients younger than 20 years had higher incidence of advanced -stage disease than adult [4,5]. More than 90% of children with nasopharyngeal carcinoma present with advanced disease (stage III/IV or T3/T4)[8-10] as designated by tumor-node-metastasis (TNM) classification system of AJCC staging. Less than 10% cases presented with distant metastases at diagnosis involving bones, lungs, liver, bone marrow and mediastinum[10,11]. Presentation with Lymph node metastases is found in majority patients. Nasopharyngeal carcinoma is strongly associated with Epstein-Barr virus (EBV) infection. In addition to serological evidence of infection in more than 98% of patients, EBV DNA is present in the nasopharyngeal carcinoma cells and EBV antigen on cell surface of tumor cell[12-14]. The circulating levels of EBV DNA (EBV-PCR) and serologic documentation of EBV infection(anti-EBV-VCA-IgA) may aid in the diagnosis as well as monitoring response to therapy[12-14]. Diagnosis of nasopharyngeal carcinoma is made from a biopsy of the primary tumor or enlarged lymph nodes of the neck. Immunohistochemistry is needed to differentiate from other types of cancer in the head and neck area. To determine the primary tumor extension visualization of nasopharynx by nasal endoscopy and magnetic resonance imaging (MRI) of the head and neck are needed. Evaluation of the chest and abdomen by computed tomography (CT) and bone scan is performed to determine whether there is metastatic disease.

Increased incidence of NPC is usually observed worldwide at age 15-19 years. In Paediatric Hematology and Oncology department of National Institute of Cancer Research & Hospital (NICRH), children up to 18 years of malignancy are treated. Moreover, NICRH is unique for implementation of combined-modality therapy. So, the center might be a hub for having paediatric malignancy cases from all over the country. Though no study is done yet to see clinical-demographic profile as well as treatment outcome of NPC among paediatric age group. We had some unique observation regarding the living areas and month of enrollment of the NPC in children. Another important issue is that Bangladesh is one of South Asian countries where NPC is endemic. These different observations inspired the investigation of the clinical and demographic profile of pediatric nasopharyngeal carcinoma.

Material and Methods

Selection of patients: This cross-sectional study enrolled all eligible patients up to 18 years of age diagnosed with nasopharyngeal carcinoma at the Paediatric Hematology and Oncology Department, from July 2016 to June 2022 of NICRH, Bangladesh. A written forms were used for data collection which includes clinical information related to age, sex, area of living, month of enrollment, clinical presentation with duration, histopathology with pathological grading & Immuno-histochemistry reports. Data were also collected from reports of all radio-imaging for tumor details as well as metastatic work-up. Due to financial constraints, the FDG-PET scan could not be done.

Histologically proven newly diagnosed cases were enrolled. Immunohistochemistry was done from all biopsied specimens of studied children. Circulating levels of EBV- DNA and or serological marker for EBV infection could be done only in very few cases.

Information related to age, sex, address, month of enrollment, clinical presentation, size of tumor (T), nodal status(N) and presence of metastases(M) were gathered from clinical as well as findings from CT / MRI of head

& neck region, imaging of chest & abdomen and Bone scan were collected. Lymph nodes were classified as invaded when diameter is >12 mm or when central necrosis or extracapsular spread is identified by MRI or CT scan. Then tumor staging was defined from Tumor-Node-Metastasis (TNM) classification system of the American Joint Committee on Cancer (AJCC, 8th edition)[15]. Grading of tumor was collected from histopathological reports. Evidence of EBV infection was supported from positivity of LMP1 by IHC report. Serological assay could be done in only few cases.

Statistical analysis: All information were recorded in a data sheet. Recorded data were edited and analyzed statistically with SPSS for Windows version 23.0 software.

Ethical consideration: Written informed consent was obtained from all patients and /or their legal guardians before taking the information details.

Results

Total 62 children were enrolled in the study from July 2016 to June 2022. The study found predominance of male (40 male; 64.5% and 22 females;35.5%) with M: F=1.8: 1 (Table I).

Table I: *Demographic & Clinical Characteristics of children with NPC (N = 62)*

Characteristics	Summary measures	Category	Frequency	Percentage
Age (in years)	Range 7.5 to 17	7.5 to <10	7	11.3
	Mean (±SD) 12.93±2.56	10 to <15	37	59.7
	Median 13.0	15 to <19	18	29.0
Sex		Male	40	64.5
		Female	22	35.5
		M:F=1.8:1		
Clinical presentation		Unilateral Neck Swelling	31	53.2
		Bilateral neck swelling	27	37.1
		Epistaxis	30	50.0
		Nasal obstruction	17	29.0
		Fever	10	16.1
		Earache & Otitis media	8	12.9
		Headache	6	9.7
		Hemoptysis	4	6.5
		Lack jaw	4	6.5
		Back pain	4	6.5
		Sinusitis	3	4.8
		Dysphagia	1	1.6
		Respiratory difficulty	1	1.6
Duration of presentation (months)	Range 1 to 12	1 to 3	27	43.5
	Mean 4.75±2.87SD	>3 to 6	24	37.7
	Median 4.0	>6 to 12	11	17.7
Degree of differentiation (G1-G4)		Moderately differentiated (G2)	2	4.8
		Poorly differentiated (G3)	34	54.8
		Undifferentiated (G4)	25	40.3
Size of tumor(T)		T1	9	14.5
		T2	12	19.4
		T3	18	29.0
		T4	23	37.1
Nodal Status(N)		N0/NX	4	6.5
		N1	25	40.3
		N2	26	41.9
		N3	7	11.3
Presence of Metastasis(M)		M0	56	90.3
		M1	6	9.7

Median age at diagnosis was 13.0 years; range, 7.5 to 17 years. The majority 59.7% (n=37) cases from 10 to <15 years age, 29.0% (n=18) at 15 to <19 years age and rest 11.3% (n=7) were in 7.5 to <10 years age group (Table I).

The study revealed that 40.3% of children came from the northern regions of the country, including districts such as Gaibandha, Thakurgaon, Panchagarh, and Netrokona. Meanwhile, 21.0% were from the southern parts, particularly Cox's Bazar. The remaining 38.7% of children were from various other regions across the country (Figure 1). NPC cases were found throughout the year 8-12 in number per year but mild increase in incidence was observed in the month of March -April 19.4%, then November - December 19.4% (Table II).

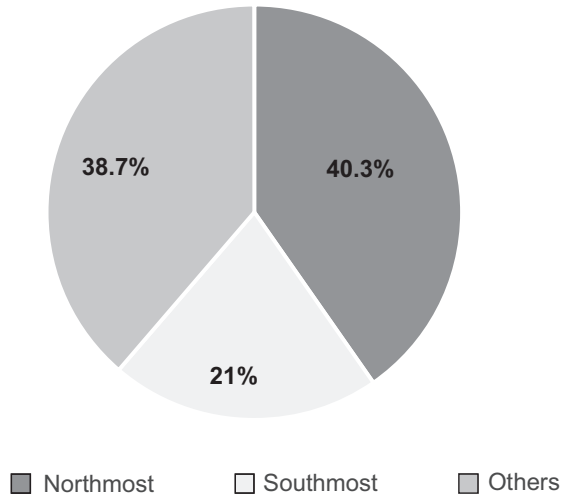


Figure 1. *Disease distribution by Areas of Living*

Duration of clinical symptoms ranged 1 -12 months with mean 4.75±2.87 SD. Median duration of clinical symptoms were 4.0 months though commonly (43.5%; n=27) presented within clinical duration of 1 to 3 months (Table I).

The most common clinical presentation was neck swelling, 90.3% (53.2% unilateral and 37.1% bilateral), followed by epistaxis (50.0%), nasal blockage (29.0%), headache (9.7%), irregular fever (16.1%), earache & otitis media (12.9%). Other less common presentations were hemoptysis 6.5%, lock jaw 6.5%, back pain for bone metastasis 1.6%, respiratory difficulty 1.6%, sinusitis 4.8%, dysphagia1.6% etc. (Table I).

Clinical profile related to size, nodal status, metastasis, and grading of tumor are described in TableI. Regarding size of tumor T4-37.1%, T3- 29.0%; T2 -19.4% and T1-14.5%. Nodal involvement as N1-40.3%, N2-41.9%, N3-11.3% and Nx -6.5%. Metastatic disease was found in 9.7% cases, where all 6 cases had vertebral metastasis (Table I).

By TNM staging of AJCC 8th edition, children studied had advanced stage disease 83.9% with stage III 41.9% (n=26), stage IVA 32.3% (n=20) and stage IVB 9.7% (n=6) and low stage II constitute only 16.1% (n=10) (Figure II).

Histopathological reports revealed that 96.8% of cases were poorly to undifferentiated histology, with only 3.2% being moderately differentiated. According to the World Health Organization (WHO) classification, the study found that 96.8% of the cases were type III or undifferentiated carcinoma among the children studied (Table I).

Table 2: *Disease distribution by Month of Enrollment (N = 62)*

Months	Frequency	Percentage
January -February	7	11.3
March-April	12	19.4
May-June	11	17.7
July-August	11	17.7
September-October	9	14.5

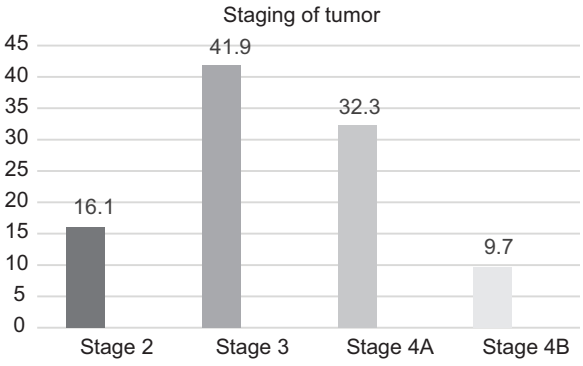


Figure 2: *Staging of Tumor by AJCC - staging System of 8th edition*

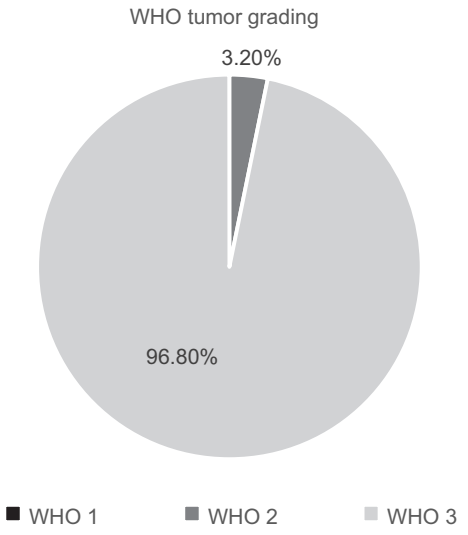


Figure 3. *WHO -grading distribution.*

Discussion:

Among enrolled 62 children, the study found male (40) predominant, with the incidence ratio between male and female was 40:22=1.8:1; which is close to some of previous studies of NPC in young patients[16,17]. Male gender is likely to be a genetic risk factor for the disease independent from environment.

Median age of the studied children was 13.0years, range 7.5 to 17 years with mean 12.93±2.56SD. Nasopharyngeal carcinoma is very rare in children younger than 10 years and increases in incidence is usually observed from aged 15 to 19 years[3-5]. On the contrary, the recent study found majority (n=37; 59.7%) cases from 10 to <15 years age group and 11.3% (n=7) from below 10 years age group. So, 71.0% (n=44) cases were from under 15 years age (Table I). This finding is completely different from SEER cancer Statistics review studies of Sultan et al., and Richard et al., who described raised trend of incidence is at aged 15 to 19 years [4,5].

Among the children studied, the NPC cases were found throughout the year but mild increase in incidence was observed in the month of March -April 19.4%, then November - December 19.4% (Table II).

But the study identified an important finding regarding the area of residence of the children. A cluster of NPC cases came from specific parts of the country—40.3% were from the Gaibandha, Thakurgaon, Panchagarh, and Netrokona districts, which are located in the northernmost part of Bangladesh, and 21.0% were from the southernmost part of the country, such as Cox's Bazar. The remaining 38.7% were distributed across various other regions of Bangladesh. The cause of this clustering is unknown and requires further evaluation, such as investigation into Epstein–Barr viral association, food habits, genetic susceptibility, etc.

By the observation of the recent study (Table1), the commonest presenting symptoms were neck node swelling (90.3%) followed by epistaxis (50.0%), nasal blockage (29.0%), irregular fever (16.1%), earache & otitis media (12.9%), headache (9.7%). These characteristics were consistent with the results of previous studies[2,7]. Less commonly studied children had also bone pain, dysphagia, sinusitis, respiratory difficulties etc. Bone pain in this study was due to vertebral metastasis by which 9.7% children presented initially. Median duration of clinical symptoms was 4 months, ranges 1 to 12 months with mean 4.75±2.87 SD. A four -month median time from onset of the presenting symptom to diagnosis indicated that most patients had a relatively long disease history before diagnosis.

Some population-based studies have reported that patients younger than 20 years had a higher incidence of advanced-stage disease than did adult patients[4,5]. Our studied children (Figure 2). had also advanced stage disease 83.9% (stage III 41.9%, stage IVA 32.3% and stage IVB 9.7%) near to some of previous studies, where more than 90% of children and adolescent with NPC presented with advanced disease[9,10, 18]. The tendency of young patients to be diagnosed at advanced stage may be attributed to factor related to the aggressive biological nature of undifferentiated tumors, which accounts for the majority children with NPC. This statement goes in favor of the histopathological reports of our NPC cases, who showed poor to undifferentiated histology in 96.8 % and only 3.2% was moderately differentiated, and by WHO classification the study found (Figure 3), 96.8 % type III or undifferentiated carcinoma among the studied children like others[4,5].

The study found majority NPC case from under 15 yrs. Fair number of children were from north-most districts of Bangladesh. Commonest clinical personation was neck swelling. Majority children are presented with advanced stage disease and WHO type III or undifferentiated histology.

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Original Article

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The Relationship Between *H. Pylori* Infection and Stomach Cancer Patients: A Cross-Sectional Study in a Tertiary Level Hospital in Bangladesh

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Abstract

Background: *Gastric cancer is the 4th most common cancer worldwide and the second most common cause of cancer-related deaths. The available treatment modalities are not satisfactory in terms of overall survival benefit. Therefore, primary prevention and early detection strategies remain the most important public health interventions. The aim of the study was to determine the role of H. Pylori Infection in stomach cancers among the patients admitted to NICRH, a tertiary-level hospital.* ***Methods:*** *This was a cross-sectional comparative study conducted at the NICRH department of medical oncology. A total of 122 patients suffering from different cancers were included in the study. H. Pylori was detected in a blood sample for H. Pylori antibody & Endoscopic biopsy.* ***Results:*** *The mean age of the gastric cancer patients was 51.8 (±12.28) years, and that of the non-gastric cancer patients was 51.43 (±12.09) years. Most of the gastric cancer patients were suffering from intestinal variant (45, 73.8%), and the remaining 16 (26.2%) patients had diffuse type. Around 38% of GC patients were diagnosed with H. pylori infection. Only 18% of patients in the non-GC group harbored the bacterium.* ***Conclusion:*** *H. pylori remains the primary carcinogen. This ancient bacterium still has a survival edge in the stomach. Effective eradication strategies of H. pylori should be strengthened.*

Keywords*: Stomach cancer, H. pylori*

Introduction

Gastric cancer is the 4th most common cancer worldwide and the second most common cause of cancer-related deaths.[1] Despite complete resection of gastric cancer and lymph nodes dissection, as well as improvement of chemotherapy and radiotherapy, there are still 700000 gastric cancer-related deaths per year worldwide and more than 80% of patients with advanced gastric cancer die of the disease or recurrence of the disease within 1 year after diagnosis. None of the treatment modalities we have been applying today can influence the overall survival rates. At present, the 5-year relative survival rate for gastric cancer is about 28% [2]. According to the International Gastric Cancer Society, more than 800,000 people are affected by gastric cancer every year, and up to 650,000 people succumb to gastric cancer [2]. It is likely that in 2030 gastric cancer will increase by 10% in developing countries. Gastric cancer remains an important burden for public health, particularly in less developed countries, including Middle and Eastern Asia, South America, and Eastern Europe, being responsible for 70% of cases worldwide [2]. Mortality rates remain high with disease usually detected late in its course; at this stage, treatment strategies are often not useful. Therefore, primary prevention and early detection strategies remain the most important public health interventions [3]. However, these strategies require the identification and understanding of risk factors that lead to carcinogenesis. With gastric cancer, a disease that is traced to ancient civilizations, the risk appears to evolve over time as a possible result of changes in dietary and lifestyle factors. Improved sanitation, refrigeration, and effective eradication strategies for Helicobacter pylori (*H. pylori*) have led to a significant reduction in the incidence of cancer in recent years. However, the fact that this disease remains prevalent in modern times suggests that other environmental risk factors may be involved in sustaining this condition. *H. pylori* is the primary carcinogen, as this ancient bacterium has a complex ability to interact with its human host.

Food that inhibits the viability, colonization, and infection of *H. pylori* may reduce the risk of cancer. Obesity is increasingly recognized as a contributory factor in gastric cardia carcinogenesis. Gender is shown to play a role in the occurrence of certain cancers. Gastric cancer is more frequent among males than females as a whole. These two subtypes present marked differences in pathology, epidemiology, etiology, and biological behavior [4]. The purpose of the Intestinal subtype gastric cancer is the most frequent globally and is particularly common in geographical regions with a high risk of the malignancy [5]. Intestinal subtype tumors are often localized in the lower part of the stomach (antrum), and are characterized by having well-defined glandular formation, similar to the microscopic appearance of colonic mucosa [6,7]. The development of intestinal subtype gastric cancer follows a stepwise sequence of precursor lesions starting with superficial gastritis, continuing through chronic atrophic gastritis, intestinal metaplasia, dysplasia, and ultimately, overt gastric cancer [8]. For unknown reasons, the multistep process often does not lead to neoplasia, as it stops at one of the stages and undergoes regression [9,10]. It is hypothesized, however, that "a point of no return" exists where the process cannot be reversed. The etiology of intestinal subtype gastric cancer is mainly associated with environmental factors, the tumor frequently develops late in life (after 50 years of age), and is twice as common in males as in females [11]. Diffuse subtype gastric cancer more commonly develops in the corpus of the stomach and is characterized by the lack of gland formation and cellular adhesion, with single/small clusters of neoplastic cells diffusely infiltrating the stroma of the stomach wall. No recognizable pre-neoplastic lesions have been observed during the development of diffuse cancers [12,13]. Diffuse subtype tumors are associated with genetic predisposition, and presumably arise out of single-cell mutations in normal gastric glands [14,15]. The diffuse subtype has a relatively constant or even slightly increased incidence rate, more often occurs in young individuals, presents a similar prevalence in males and females, and is associated with a worse prognosis than the intestinal subtype [11,16]. The anatomical location of tumors in the stomach has also been considered as an important parameter for the classification of gastric cancer [17]. On the basis of anatomical location two subtypes of gastric cancer can be distinguished: tumors from the distal regions of the stomach (non-cardia cancer) and those arising at the most proximal part of this organ (cardia cancer) [17]. These two anatomical subtypes of

tumors present remarkable etiological differences. Non-cardia cancer is generally thought to develop as a result of the interaction between environmental, host and *H. pylori* factors. In contrast, two distinct etiological mechanisms have been proposed for cardia gastric cancer. One is associated with atrophic gastritis and resembles the development of non-cardia malignancies. The second arises in a similar fashion to esophageal carcinomas, as a result of frequent refluxing of acidic gastric juice into the distal esophageal mucosa, which leads to the transformation from squamous to columnar metaplastic epithelium to, ultimately, overt cancer [7,9,10]. Epidemiological dissimilarities also exist between these two anatomical subtypes of gastric tumors. Non-cardia gastric cancer accounts for the majority of the cases worldwide and is the predominant type in high-risk areas. In contrast, cardia cancer is more homogeneously distributed all over the world and its incidence tends to increase[17,18]. The study aimed to determine the relationship between *H. Pylori* infection, which might induce the development of gastric cancer, the most frequently encountered type of gastrointestinal cancer in Bangladesh.

Materials and Methods

It was a comparative cross-sectional study carried out in the National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka. This study period was fifteen (15) months, from January 2023 to March 2024. The subjects were selected using a Purposive sampling technique. The targeted sample size = 61. An equal number of other patients not suffering from gastric cancer were also included in the study for comparison. *H. Pylori* was determined by a blood sample for H. Pylori antibody & Endoscopic biopsy. After obtaining the necessary permission, the researcher collected data from the patients through face-to-face interviews. Relevant medical records were consulted and recorded in a semi-structured questionnaire.

Results

This cross-sectional study was done to determine the relationship between *H. Pylori* infection and stomach cancer in patients admitted to NICRH. Hundred and twenty-two patients were included in the study. Of the 61 were suffering from gastric cancers. Another 61 patients of non-gastric cancers (Lung cancer 17, 27.9%, Lymphoma 15, 24.6%, Sarcoma 11, 18%, Seminoma 9, 14.7%, Cervical cancer 5,8.2%, and other cancers 4, 6.6%) were also enrolled in the study. The findings derived from the data analysis are presented in this section.

Figure 1 shows the age distribution of the patents. The mean age of the gastric cancer patients was 51.8 years and that of the non-gastric cancer patients was 51.43 years. No significant difference was observed between these two groups; $p>0.05$).

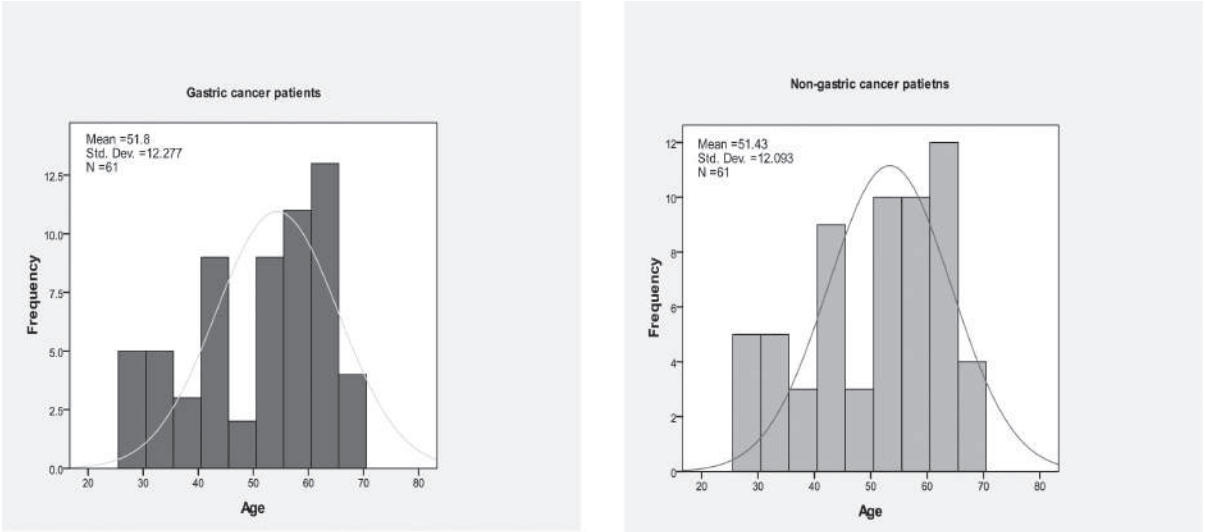


Figure 1: *Age distribution of the patients*

Table I: *Distribution of the patients by Gender*

Sex	Category		χ^2	*p*-value*
	GC (n=61)	Non-GC (n=61)		
Male	48 (78.7)	50 (82.0)	0.207	0.649
Female	13 (21.3)	11 (18.0)		

GC= Gastric cancer; Percentage is given in parentheses

The current study included 48 (78.7%) male and 13 (21.3%) female gastric patients. Almost similar numbers of male (50, 82%) and female (11, 18%) non-gastric cancer patients were included in the study. Statistically, the difference was not significant (p>0.05) (Table I).

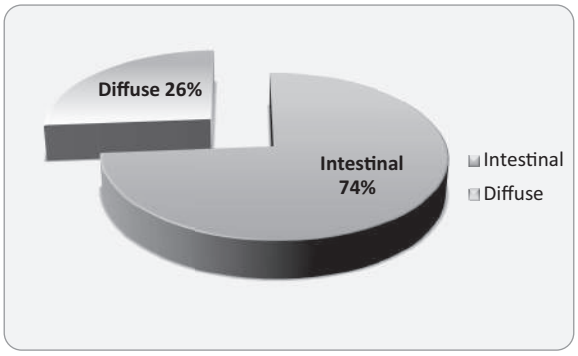


Figure 2: *Histological types of gastric cancer (n=61)*

Figure 2 shows the histological types of gastric cancer. Most of the gastric cancer patients were suffering from intestinal variant (45, 73.8%), and the remaining 16 (26.2%) patients had diffuse type.

Table II: *Distribution of the patients by H. pylori infection*

H. pylori **infection**	Category		χ^2	p-value*
	GC (n=61)	Non-GC (n=61)		
Yes	23 (37.7)	11 (18.0)	5.872	0.015
No	38 (62.3)	82.0)		

GC= Gastric cancer; Percentage is given in parentheses

Around 38% GC patients were diagnosed with *H. pylori* infection. Only 18% of patients in the non-GC group harbored the bacterium. Statistically, this difference was significant (p<0.05) (Table II).

Table III
Binary logistic regression analysis of risk for gastric cancer

Risk for gastric cancer	Odds Ratio (OR)	Confidence 95% Interval (CI)	
		Lower	Upper
H. pylori infection	2.7	1.2	4.7

The above table (Table III) presents a binary logistic regression analysis of the risk of gastrics cancer. H. pylori infection was associated with an increased risk of gastric cancer (OR: 2.7).

Discussion

The current study was conducted at the National Institute of Cancer Research and Hospital to determine the relationship between *H. pylori* infection and stomach cancer in patients admitted for treatment.

Gastric cancer remains an important burden for public health, particularly in less developed countries including Middle and Eastern Asia, South America and Eastern Europe, being responsible for 70% of cases worldwide[2]. Mortality rates remain high with disease usually detected late in its course; at this stage treatment strategies are often not useful. Therefore, primary prevention and early detection strategies remain the most important public health interventions[3]. However, these strategies require identification and understanding of risk factors that lead to carcinogenesis.

Improved sanitation and effective eradication strategies of Helicobacter pylori (*H. pylori*) have led to a significant reduction in the incidence of this cancer in the recent past [19] but the fact that this disease remains prevalent in modern times suggests that other environmental risk factors are involved in sustaining this condition.

The risk of non-cardia but not cardia gastric cancer increases with higher intakes of total, red and processed meat in *H. pylori*-infected subjects, with an absolute risk of 0.3% in ten years in those having the highest quartile of total meat intake[20]. Before 1984, peptic ulcer disease as a global public health burden, was assumed to be associated with acid and stress [21,22]. Marshall & Warren in 1984 were the first to describe the association between peptic ulcer disease and H. pylori, and it has since been associated with gastric cancer [23] as well. In our study, both the prevalence of PUD and *H. pylori* infection were higher among GC patients.

There is strong evidence for *H. pylori* being a class I carcinogen that causes gastric cancer [24,25]; its eradication has since resulted in hope for the control of this debilitating disease[26]. Developed countries, including Australia, that have improved socio-economic and living conditions during the formative years of their populations have reported both a lower prevalence of H. pylori and incidence of gastric cancer[27].

The eradication of infection in clinical trials, with the aim of reducing cancer incidence, has been somewhat inconclusive[26]. Notwithstanding, these studies suggest that *H. pylori* is only a triggering factor in this multi-step disease, and that *eradicating H. pylori early in life is crucial* for disease prevention to be successful.

In the current study, most of the gastric cancer patients were suffering from intestinal variant (45, 73.8%), and the remaining 16 (26.2%) patients had diffuse type. It is a well-known fact that the intestinal type is more prevalent in men, in older age, and the etiology is predominantly environmental. Whereas, diffuse type is more common in women, in younger individuals, and its etiology is mainly familial.

The risk of non-cardia but not cardia gastric cancer increases with higher intakes of total, red, and processed meat in *H. pylori*-infected subjects, with an absolute risk of 0.3% over ten years in those with the highest quartile of total meat intake[20].

Conclusion

Gastric cancer is one of the most common malignancies worldwide. Despite its declining incidence in developed countries, *H. pylori* remains a significant public health burden, likely sustained by environmental risk factors, both known and unknown. *H. pylori* is the primary carcinogen. Although its prevalence has decreased markedly due to improved sanitation and effective eradication strategies, this ancient bacterium still has a survival advantage in the stomach.

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Original Article

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Utility of Risk of Malignancy Index (RMI) in Predicting Malignancy in Patients with Adnexal Mass-Experience in A Tertiary Hospital

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Abstract

Background*- Ovarian malignancy is one of the silent killers as most of the cases present in advanced stages. Pre-operative assessment regarding the nature of adnexal mass is necessary in order to make a standard management plan. Risk malignancy index (RMI) is a simple scoring system based on three factors - serum CA -125, USG score and menopausal status. The objective of the study was to evaluate risk malignancy index (RMI) in pre-operative prediction of malignancy in women with adnexal mass.* ***Materials and Methods****: This was a cross-sectional study. Study population was patients with clinical or radiological diagnosis of adnexal mass who were admitted under gynecological oncology department of NICRH for surgery between July 2022 and June 2023. Information on demographic characteristics, ultrasound findings, menopausal status, preoperative CA125 level, and post operative histopathology was collected. Sensitivity and specificity of each parameter of RMI (menopausal status, USG score and CA 125 level) was measured. RMI score for each patient was calculated. ROC curve was constructed to find predictive power of RMI level in detecting malignant adnexal mass and to find best cut off value.* ***Results****: Total 57 patients were enrolled for the study. 38 (66.7%) cases were found to be malignant in postoperative histopathological reports. Analysis of the individual parameters of RMI revealed that menopausal status, raised CA 125 level (> 35 IU/ml) and ultrasound score were not good predictors of malignancy individually (sensitivity and specificity 47.4%,63.2%; 84%,43% and 65.8%, 78.9% respectively). RMI level >200 had good sensitivity and specificity of 82% and 79% with AUC .839 in predicting malignancy in adnexal mass. Conclusion: RMI is highly reliable tool in differentiating benign and malignant ovarian lesions. A cut-off of 200 may be suitable for triaging patients with adnexal mass and early referral to tertiary care centers.*

Keywords: *Adnexal mass, Malignancy, RMI*

Introduction

Internationally, ovarian cancer is the 8th common female cancer worldwide. In Bangladesh there were 3122 new cases, and total death was 2096[1] in 2022. It is often called the "silent killer" because the disease is not often detected until it reaches advanced stage due to anatomical location of ovaries and lack of screening tools.

An adnexal mass is one of the most frequent indications for referral to specialist gynecologists. Management of malignant masses are different than that of benign and require referral to special center. Up to 24% of ovarian tumors in premenopausal women are malignant and up to 60% are malignant in postmenopausal women[2]. Preoperative evaluation and discrimination of adnexal masses as benign and malignant is of utmost importance and play central role in decision making regarding - clinical management and proper surgical planning of patients. There should be a standardized and available method specially for rural areas for this purpose. This will allow optimization of first-line treatment for women with ovarian cancer.

Patients with suspected ovarian malignancy should be referred to gynecological oncologists, for treatment planning, proper preoperative evaluation, choosing proper surgical procedure and improving the quality of cytoreductive surgery. Accurate per operative surgical staging and optimal cytoreduction are important prognostic factors in ovarian malignancy. Oncological outcome of ovarian cancer is largely dependent on its surgical management[2,3]. On the other hand, unnecessary referral of benign cases to tertiary oncology center increases burden to these centers. So timely and appropriate evaluation of adnexal masses and referral of the suspected patients to a gynecological oncologist is important and has been proven to improve outcome of patients with ovarian cancer[4].

Currently standard workup for evaluation of adnexal mass includes clinical examination, imaging assessment, tumor markers assay. In most cases, however, history and physical examination alone are insufficient to make a diagnosis, and ultrasound imaging, with or without laboratory studies, is necessary. The ultimate diagnostic tool is histological examination.

Various diagnostic tests for evaluation of adnexal mass are available to date, but they are not very dependable due to low diagnostic performances. The commonly available tests are tumor markers and radiological imaging methods. Serum CA125 level is often used for distinguishing malignant tumors in case of adnexal pathology. But CA -125 level has limited value as individual parameter as it is elevated mostly in advanced stage (92%) ovarian malignancy and only 50% cases in early stage tumors[5]. Though IOTA simple rule has emerged as promising tool for predicting malignancy, it is inconclusive in about 25% cases[6]. MRI has excellent soft tissue resolution with high accuracy[7] for evaluation of adnexal mass. But it is expensive and unavailable in many peripheral areas-that makes it unsuitable for routine use. Risk of malignancy algorithm (ROMA) is a recent test, which combines the serum CA 125 and HE4 with menopausal status into a numerical score. But HE4 is currently not available in all peripheral areas of Bangladesh, and it requires a complicated calculation[8].

To reduce the diagnostic dilemma between benign and malignant ovarian masses, a formula-based scoring system - risk of malignancy index (RMI) was introduced in 1990[9-12]. Jacobs et al. originally developed the RMI, which is now termed RMI1.Tingulstad et al. developed their version of the RMI in 1996, and it is known as RMI 2. In 1999, Yamamoto et al[13] further modified RMI 2, which is termed as RMI 3. Risk of malignancy index (RMI) is a diagnostic model with combined parameter. RMI is calculated with a simplified regression equation obtained from the product of menopausal status score (M), ultrasonographic score (U), and absolute value of serum CA-125[10-11].The main advantage of RMI is that it is a simple and objective scoring system that can be applied directly into clinical practice with simple set up, without the necessity of expensive or complicated methods (such as computed tomography scan, magnetic resonance imaging and whole-body emission tomography). As all parameters (menopausal status, CA 125, USG) are available in all areas, this is a suitable method of evaluation of adnexal masses in peripheral areas where it is much needed. A systematic review in 2009 concluded that the risk of malignancy index is the best available test to triage patients with ovarian tumors for the referral to the gynecologic oncologist.[13]

The aim of this observational study was to evaluate the role of Risk of Malignancy Index (RMI) in differentiating benign and malignant ovarian masses preoperatively.

Methodology

This study was observational cross- sectional study which was conducted in gynecological oncology department of National Institute of Cancer Research and Hospital, Dhaka. A total of 57 patients within a period of 12 months from July 2022 to June 2023, who attended the outpatient department with radiological or clinical evidence of an adnexal mass and for whom surgical treatment was planned, were included in the study. Patients below 18 years or who had evidence of obvious malignancy (ie-extensive metastases in imaging or biopsy proven malignancy or prior history of taking chemotherapy) were excluded from study. Detailed history was taken and for each patient trans abdominal and transvaginal USG with color doppler was performed. Obtained data included: age, menopausal status, clinical features at presentation, ultrasound findings and CA125 levels. RMI 3 was calculated for all patients. The RMI-3 was calculated using the formula RMI=M x U x serum CA- 125 where (M) refers to the patient's menopausal status, (U) refers to the ultrasound score and serum (CA -125) was the assayed level expressed in U/ml.

Postmenopausal status is defined as more than 1 year of amenorrhea. A score of M=3 is given to postmenopausal women and M=1 for premenopausal status.

5 ml of venous blood was collected for serum CA-125 estimation. Abnormal CA 125 level is defined as serum level ≥35 U/mL.CA 125 level was entered directly into the equation. For USG score calculation-patients were evaluated by trans abdominal or transvaginal ultrasonography in the radiology and imaging department of this institute. Adnexal masses were evaluated for five sonographic morphological criteria – presence of solid structure, bilaterality, presence of ascites, presence of metastasis and multilocularity. If there is presence of 1 or no feature- USG score will be 1 and in presence of two or more feature- USG score will be 3.

Total score was calculated for each patient.

After surgery specimen was sent for histopathological examination.

Postoperative histopathology of all the cases was collected, and patients were classified as benign and malignant group. Borderline tumors were included in malignant groups. Histopathological findings correlated with RMI score. The diagnostic performances of three parameters of RMI and RMI score, were evaluated in sensitivity, specificity, NPV, and PPV. Histopathology report was considered as gold standard.

Result

The study included total of 57patients. Distribution of cases by age and their distribution of histopathological category (benign and malignant) is shown in Table1. The age of the patients varied from 18 to 79 years (mean, 43.16 years). 33(58%) patients were in age group >40 years and 42% patients are <40 years. Out of 16, 6 patients (37.5%) had malignant disease in age group <30, Age group 31-40 had minimum portion (25%) of malignant disease Malignant disease picked in the age group 41-50. 50% of patients in this age group were diagnosed as malignant. Majority of patients are premenopausal (56.14%).

Table 1: Age group distribution of the patients(n=57)

Age group (yrs.)	Malignant	Benign	Total
d"30 (n, %)	6 (37.5)	10 (62.5)	16 (100.0)
31-40 (n, %)	2 (25)	6 (75)	8 (100.0)
41-50 (n, %)	4 (50.0)	4 (50.0)	8 (100.0)
51-60 (n, %)	5 (27.8)	13 (72.2)	18 (100.0)
>60 (n, %)	2 (28.6)	5 (71.4)	7 (100.0)

Based on postoperative histopathological examination reports, 38 patients (66.7%) had malignant tumors, and 19 patients (33.3%) were diagnosed as benign (Table 2). Serous cystadenoma and endometriotic cyst were common benign tumors. Each of these types were found in 6 cases. Dermoid cyst and mucinous cystadenoma were next common benign types. Serous cystadenocarcinoma was common malignant tumor. Out of 38 malignant cases 23 patients (63%) were serous cystadenocarcinoma. Next common type was mucinous cystadenocarcinoma. Malignant germ cell tumor and low-grade serous tumor were found in 3 and 2 cases respectively.

Among 57 patients, 25 patients are postmenopausal, and 32 patients are premenopausal. Benign cases are more frequent in premenopausal (21.05% vs 35.09%) than postmenopausal (12.2% vs 31.58%).

Table II: *Distribution of patients according to histopathological findings*

Histopathologic diagnosis	Frequency
Benign cases (19)	
Serous cystadenoma	6
Endometriotic cyst	6
Dermoid cyst	4
Mucinous cystadenoma	3
Malignant cases (38)	
Serous cystadenocarcinoma high grade	23
Serous cystadenocarcinoma low grade	2
Mucinous cystadenocarcinoma	7
Malignant germ cell tumour	3
Malignant brenner tumour	1
Clear cell adenocarcinoma	1
Borderline tumor	1

RMI scores of patients varied from 12 to 20700 (mean, 1874±3196.3). Figure 1 shows distribution of patients according to RMI status. Total 34(59.65%) patients had RMI score ≥200. Among them (within 59.65%) 52.63% were malignant and 7.02% were benign. On the other hand,23(40%) patients had RMI level<200. Majority of patients (26.32% vs 14.04%) were benign when RMI score <200.

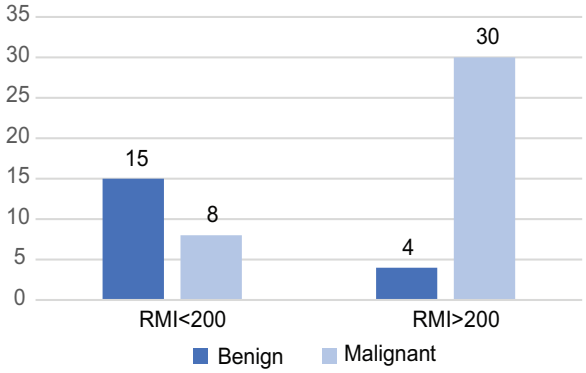


Fig.-1: *Distribution of histopathological nature according to RMI value(n=57)*

The serum CA125 levels in the patients varied from 4 to 7500 U/mL (mean, 491.88 U/ml).

Table III shows individual performances of three parameters of RMI (CA-125, menopausal statis, USG scoring) in prediction of malignancy. Out of 57, 42 patients had their preoperative serum CA 125 level >35 U/ml (Table III). Among them 32 (76.19%) patients were found to have malignant disease and 10 (23.8%) had benign disease in postoperative histopathology. 9 out of 15 patients (60%) patients with CA125 levels less than 35U/mL had benign lesions. Sensitivity, specificity, PPV and NPV of raised CA 125 (>35 u/ml) in detecting malignancy is 84.2%, 47.4%, 76.2% and 60%.

Table 3: *Predictive values of USG score, CA 125 and RMI scores and menopausal status of malignant and benign lesions(n=57)*

Variables	Malignant	Benign	Sn (%)	Sp (%)	PPV (%)	NPV (%)
Premenopausal	20	12	47.4	63.32	72.0	37.5
Postmenopausal	18	07				
USG score 1	13	15	65.8	78.9	86.2	53.6
USG score 3	25	04				
CA 125 ≤35	06	09	84.2	47.4	76.2	60.0
CA 125 > 35	32	10				
RMI ≤200	08	15	81.9	78.9	88.2	65.2
RMI >200	30	04				

The performance of USG score 3 as an individual factor in predicting malignancy was analyzed. USG score 1 and 3 were found in 28 and 29 cases respectively. Among 29 cases who have USG score 3, 25 were found malignant postoperatively and 4 are benign. Sensitivity of USG score was 65.8% and specificity 78.9% (table-3) as predictor of malignancy. The positive predictive value was 86.2% and negative predictive value was 53.6 % for this parameter in the present study.

In present study sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of menopausal status in predicting adnexal malignancy are calculated which are 47.4%, 63.32%, 72% and 37.5% respectively.

Comparing as individual predictive performances of the three criteria, an ultrasound score of 3 had the highest specificity in detecting adnexal malignancy (78.9%), while a raised CA 125>35 had the highest sensitivity (84.2%).

Total 34 (59.65%) patients had RMI score e"200, where 52.63% were malignant and 7.02% were benign. On the other hand, majority of patients (26.32% vs 14.04%) were benign when RMI score <200 (Table-III).

To find out the RMI value that could most effectively classify the disease, we calculated the sensitivity, specificity of RMI cut-off levels of 100, 150, 200, and 250. A comparison of the diagnostic indices with these cutoffs is shown in Table 4. As shown in this table, an RMI score of 200 had the ideal combination of sensitivity (81%), specificity (79%). Lower cut-off values of 100 and 150 showed higher sensitivity (86% & 84% respectively) in detecting malignant disease. But these values had lower specificity (58% and 74% respectively) compared to cut off 200. RMI value 250 showed higher specificity (85%) but lower sensitivity (78%).

Table IV: *Diagnostic performance of the different RMI cut-offs*

RMI cut off	Sensitivity(%)	Specificity(%)
100	87	58
150	84	74
200	81	79
250	76	84

A receiver operating curve was plotted (Fig. 2) to find sensitivity and specificity of different RMI point and to identify best RMI cut off value in predicting adnexal malignancy. Area under curve (AUC) was .89. So, RMI as a diagnostic test has high discriminatory power to differentiate benign and malignant ovarian masses. RMI level 200 was found to be best cut off point with sensitivity 81% and specificity 79%.

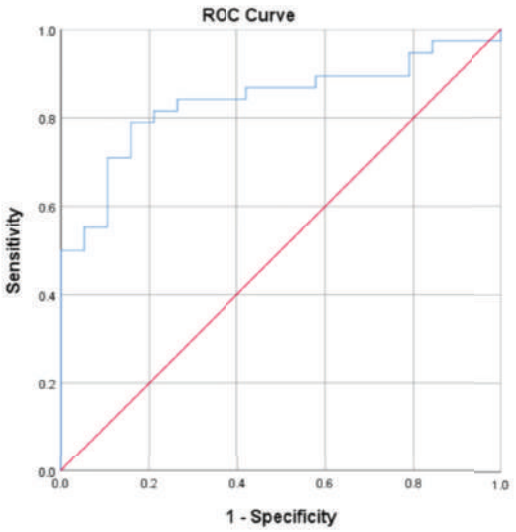


Fig.-2: *The ROC curve for RMI level*

To see the predictive power of RMI in detecting malignancy in adnexal mass a ROC curve was constructed

Discussion

Ovarian cancer has aggressive clinical course, mainly due to late diagnosis and lack of effective diagnostic tool for early-stage detection of the disease. This cross-sectional study was conducted in Gynecological Oncology department of National Institute of Cancer Research and Hospital. The objective of this observational study was to evaluate utility of Risk of Malignancy Index (RMI) in differentiating benign and malignant ovarian masses preoperatively. Fifty-seven patients with adnexal masses who were planned for surgery between July 2022 to June 2023, were enrolled in the study. Among them based on postoperative histopathological examination reports, 38 patients (66.7%) had malignant tumors and 19 patients (33.3%) were diagnosed as benign. Some other studies, like

Yamamoto et al.[13] study and Jenitha et al. study[14] showed majority patients were benign (84.2%). Majority of patients were malignant in this study as our center is a tertiary oncology referral center. Serous cystadenocarcinoma was most common malignant tumor in this study (23 out of 38 malignant cases). Next was mucinous adenocarcinoma. Serous cystadenoma and endometriotic cyst (both 6 in number) were common benign tumor types. Dermoid cyst was next common type. This result is compatible with Jenitha et al[14] study. Serous cystadenoma (28%) was the most frequent benign tumor and serous cystadenocarcinoma was 2nd most common malignant tumor in their study after mucinous adenocarcinoma.

Chance of ovarian mass to be malignant is more common in postmenopausal women in comparison to premenopausal group. In our study premenopausal women had more chance of benign lesion (12% vs 7%) in comparison to postmenopausal women. These data seem to agree with earlier Aziz et al. study [15]. Jenitha et al.[14] study also showed more frequency of malignancy among postmenopausal women (16% vs 42.4%)

Higher age is one of the risk factors for ovarian malignancy. In this study mean age of malignancy was 56 years and mean age for benign disease was 38 years. Incidence of malignancy was picked in the age group 41-50, while most frequent for benign group was 31-40 years which had least chance of malignancy (25%). Aziz et al[15] study had also shown highest occurrence of malignancy in this age group. Rate of malignancy was highest (7.4%) in this group in her study. Another recent study[16] also showed 40-51 to be pick age group for malignancy.

Serum CA125 level is widely appreciated as a useful biomarker for estimating the risk of ovarian cancer, though other gynecological pathology can also increase its levels. It is more significant in postmenopausal females as compared to premenopausal females as it can be raised in various benign conditions in before menopause.

Myers et al.[17] have earlier reported sensitivity and specificity of less than 80%, for this marker, in the prediction of ovarian cancers. Simsek et al[18] reported a sensitivity of 78.6% and specificity of 63.5% for a CA125 cut-off of 35 U/ml.

In this study CA125 >35 IU/L was found to be highly sensitive (84.2%) in detecting adnexal malignancy, though specificity was low 47.4%. Reason for low specificity in different studies is due to rising of CA 125 in different benign adnexal lesion. In Amarjeet Kaur et al. study, they have got almost similar results. In that study, sensitivity of CA 125 in diagnosing malignancy was 90.91% and specificity was 57.89%. The positive predictive value was 55.56% and negative predictive value was 91.67% [19].

In RMI scoring there are five ultrasonographic features. Scoring 3(presence of 2 or more out of 5 sonographic features) has found to have low sensitivity 65.8% and moderate specificity 78.9% with PPV 86.2, NPV 53.6 as independent factor in detecting malignancy. In another study[20] USG score had a sensitivity of 76.4 % (52.74–90.44), a specificity of 75.6 % (60.66–86.17), a positive predictive value of 56.5 %, and a negative predictive value of 88.5 % . In Aziz et al. study[15]sensitivity and specificity were 78.3% and 81.5% respectively. Specificity of RMI USG score 3 of these studies are almost similar to our study specificity. Less sensitivity of this feature in this study may be due to small sample size.

Diagnostic accuracy of RMI value > 200 in predicting adnexal malignancy was calculated (Table IV). This parameter was found to have high sensitivity and specificity which was 81% sensitive and 79% specific with high PPV (88.2%) and NPV (65.2%) in detecting malignant adnexal mass. A receiver operating curve was plotted(figure-3) to find sensitivity and specificity of different RMI point and to identify best RMI cut off value in predicting adnexal malignancy. Area under curve (AUC) was .89. So, RMI is a good test to differentiate benign and malignant ovarian masses. RMI value 200 was found to be best cut off point with sensitivity 81% and specificity 79%.

In Malla study[21] sensitivity 87.5, specificity 91.3, PPP 73.6 and NPV 96.5 for RMI score >200 (value = 0.0001), while in another study by Kaur et al.[19], the sensitivity of RMI 3 to detect malignancy in adnexal pathology – 100, specificity was 91.89%, positive predictive value was 78.57%, negative predictive value was 100%.

Predictive performances of different RMI cut-off were compared (table-V). To find out the RMI score that could most effectively classify the disease, we calculated the

sensitivity, specificity of RMI cut-off levels of 100, 150, 200, and 250. As shown in this table, an RMI score of 200 had the ideal combination of sensitivity (81%), specificity (79%). Lower cut-off values of 100 and 150 showed higher sensitivity (86% & 84% respectively) in detecting malignant disease. But these values had lower specificity (58% and 74% respectively) compared to cut off 200. RMI value 250 showed higher specificity (84%) but lower sensitivity (76%). In Aliya et al. study[15] RMI cut-off 250 was found to have best predictive performance (54.05% sensitivity 93.4% specificity).

A receiver operating curve was plotted (Fig. 3) to find sensitivity and specificity of different RMI value and to identify best RMI cut off value in predicting adnexal malignancy. Area under curve (AUC) was .89. So, RMI is a good test to differentiate benign and malignant ovarian masses. RMI level 200 was found to be best cut off point with sensitivity 81% and specificity 79%.) In another study by Karimunnisha et al.[22] the best performance obtained for RMI-3 was at the cut-off point 236 with a sensitivity of 72.5%, a specificity of 98.2%, a PPV of 98.1%.

In this study, among the parameters of RMI, CA125 as an individual parameter had good sensitivity. On the other hand, USG score 3 was found to have good specificity. Postmenopausal status as individual feature had both low sensitivity and specificity. As a predictor of malignancy of adnexal mass, RMI with cut-off >200 was found to be a sensitive tool with high specificity, PPV and NPV.

Conclusion:

It is concluded from the study that RMI with cut-off >200 has high sensitivity and specificity for differentiating benign from malignant adnexal masses preoperatively. RMI is a simple, feasible, objective diagnostic tool for preoperative prediction of malignancy in patients with adnexal mass thus providing the patients a chance for early referral, treatment, and better survival rate.

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Original Article

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Comparison of Toxicities between Weekly Versus Three-Weekly Administration of Paclitaxel as Neoadjuvant Chemotherapy in HER2-Negative, Stage-III Breast Cancer

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Abstract

Background: *One of the standard neoadjuvant chemotherapy regimens for treatment of locoregionally advanced breast cancer is doxorubicin and cyclophosphamide followed by a taxane (AC followed by T). Paclitaxel, a taxane can be given either as three-weekly or weekly schedule. The aim of this study was to compare the acute toxicities of three-weekly paclitaxel with weekly paclitaxel in the treatment of HER2 negative, stage III breast cancer.*

Methods: *A Quasi-experimental study was conducted from April 2022 to October 2023 in two centers of Bangladesh. Sixty-six patients were enrolled and divided equally into two arms. Arm-A received 4 cycles AC followed paclitaxel 175 mg/m^2 three-weekly for 4 cycles. Patients in Arm-B received 4 cycles AC followed by paclitaxel 80mg/m^2 weekly for 12 weeks. Each patient was evaluated during and after the completion of the chemotherapy to assess acute toxicities according to CTCAE version 5.0.*

Results: *Grade-1 anemia was more in arm-A (57% vs 33%), grade-2 was more in arm-B (60% vs 40%). Sixteen patients (53%) had grade-2 leucopenia in both arms. Garde-3 leucopenia and febrile leukopenia were 6(20%) and 5(16.67%) in arm-A, and 4 (13.34%) and 2(6.67%) in arm-B, respectively. Two patients (6.67%) in arm-A and 1(3.34%) in arm-B developed grade-3 diarrhea. Frequency of neuropathy were – grade-2: 7(23.33%) vs 11(36.67%); grade-3: 2(6.67%) vs 4(13.33%) in arm-A and B respectively. Although more patients on Arm-A had grade 2 or 3 toxicities numerically, none of the differences between the arms were significant (p>0.05).*

Conclusion: *The weekly schedule of paclitaxel had comparable hematological and non-hematological toxicities to the three-weekly schedule.*

Keywords: *Neoadjuvant chemotherapy, Breast cancer, Weekly paclitaxel, HER2 negative, Stage III breast cancer, Toxicity*

Introduction

According to the GLOBOCAN database breast cancer is now the leading cause of cancer death by far among women. Among all cancer deaths in 2022, almost 7% was from breast cancer with more than 2 million new cases. There is a rise in its incidence in Asia too. More than a million new cases occurred in Asia in 2022 alone which accounted for more than 45% of new cases worldwide[1,2]. In Bangladesh, it is the most common in terms of incidence and second most common in terms of cancer related mortality in females[3]. Although most patients in Western countries are diagnosed early, in less developed countries about 60% of patients have locally advanced or metastatic disease at the time of diagnosis[4]. The scenario is somewhat similar in Bangladesh.

Though exact etiology is unknown, there are a number of recognized risk factors of breast cancer. A majority of patients can develop breast cancer without any identifiable risk factor. It can occur at any age but the risk increases significantly with age. Other risk factors are – certain genetic mutations (e.g. those involving *BRCA1, BRCA2, CHEK2, PALB2, ATM, TP53, BARD1, CDH1, PTEN*), lobular carcinoma in situ, history of atypical hyperplasia in breast, other proliferative breast diseases, radiation exposure at chest before 30 years of age, positive family history, early menopause, late menarche, nulliparity, first child after 35 years age, hormone replacement therapy, obesity etc[5].

Neoadjuvant chemotherapy is the standard approach in locally advanced disease. It is used mainly to aid surgical resectability. It also plays a vital role to prevent micrometastasis. Many studies showed that pathological complete response to neoadjuvant chemotherapy is associated with significant improvement of disease-free survival and overall survival. This association varies depending upon the luminal subtypes[5,6].

The best regimen for neoadjuvant chemotherapy in HER2-negative breast cancer patients is not optimally established yet. It is assumed that regimens with proven effectiveness as adjuvant setting might also be used in neoadjuvant setting[7]. Many regimens that are currently used in neoadjuvant setting in breast cancer are based on the evidence of their proven benefit in adjuvant or metastatic setting. A commonly used regimen in our country is combination therapy with doxorubicin (A) and cyclophosphamide (C) followed by three weekly paclitaxel. Studies had showed that taxanes as neoadjuvant chemotherapy has proven benefit on survival outcomes[4]. A relatively new concept is administration of paclitaxel in a weekly schedule with a 'dose density' approach. Several studies have shown efficacy of this approach[8,9]. But the question of which approach is better is still to be settled. Green et al. (2005) showed that paclitaxel administered weekly was associated with higher pathological complete response (pCR) than administered as three-weekly[10]. Saparano et al (2015) showed that in a long term follow up, weekly Paclitaxel was proven to be most efficient regimen in TNBC patients[11]. Multiple other studies have associated this approach with less or comparable or increased acute toxicities compared with conventional schedule of paclitaxel[5, 7].

Since no previous study was carried out to compare the toxicities of these two regimens in our country's perspective, the present study may aid in optimizing the neoadjuvant chemotherapy schedule in breast cancer in Bangladesh.

Methods

This quasi-experimental study was conducted from April 2022 to October 2023 at two centers in Dhaka, Bangladesh – the Department of Clinical Oncology, Bangladesh Medical University (BMU) and at the National Institute of Cancer Research and Hospital (NICR&H). Ethical approval was obtained from respective institutions before conducting the study. Informed consent was obtained from each patient before enrollment in the study. Data were collected using a pre-made questionnaire by face-to-face interviews with patients and from their investigation reports.

Patients

Female patients of Stage-III breast cancer were enrolled in this study after histopathological confirmation, immunohistochemistry and staging workup during the mentioned period. Patients with Eastern Cooperative Oncology Group (ECOG) performance status of more than two and patients who underwent surgery of the primary site (excluding diagnostic biopsy) were excluded. Disease progression, occurrence of unacceptable toxicity, and wish of the patients were criteria for discontinuation of treatment.

Intervention

Sixty-six patients were divided equally into two arms (Arm A and Arm B) by purposive sampling.

Patients in both arms were initially treated by doxorubicin (A) 60 mg/m^2 IV on day 1 and cyclophosphamide (C) 600 mg/m^2 IV on day 1 for four cycles[6]. Then, patients of arm A were treated by paclitaxel 175 mg/m^2 by IV infusion over 3 hours three weekly for 4 cycles[6]. Patients in arm B received paclitaxel 80 mg/m^2 by IV infusion over 1 hour weekly for 12 weeks[6]. All the

patients in two arms received chemotherapy with all necessary premedications and other precautions. Patients got prefilled syringe of filgrastim 30 MIU subcutaneously when indicated. All patients completed their planned chemotherapy schedule.

Assessment

Sixty-three patients completed the planned chemotherapy schedule. One patient in arm-A and one patient in arm-B didn't continue the treatment. Two patients in arm-A and one patient in arm-B were lost to follow up. Thus, ultimately 60 patients, 30 in each arm, were analyzed. Each patient was closely monitored during and after each cycle of chemotherapy. After four cycles, first comprehensive follow-up with history, physical examination and relevant investigations were carried out to assess clinical response. At the end of the chemotherapy in both arms, second comprehensive follow up was carried out using history, physical examination and relevant investigations.

Acute toxicities (when present in any cycle) were recorded using the 'Common Terminology Criteria for Adverse Events' version 5.0 (CTCAEv5.0). For a patient, when any toxicity developed in multiple cycles of treatment, the highest grade was taken for statistical analysis. Toxicities were managed with conventional treatment and the patients were kept in close follow up subsequently. Quality of life was assessed by ECOG performance scale.

Data were analyzed according to the objectives of the study by using the SPSS (Statistical Package for Social Science) software program for Windows, version 26.0. The statistical data were analyzed by chi-square test, independent T-test and Fisher exact test where applicable. The p-value less than 0.05 was taken as significant. The entire process in depicted as a flow chart in figure-1.

Results

A total of sixty patients, distributed equally into two arms, were finally analyzed for this study. Table-1 summarizes their baseline characteristics.

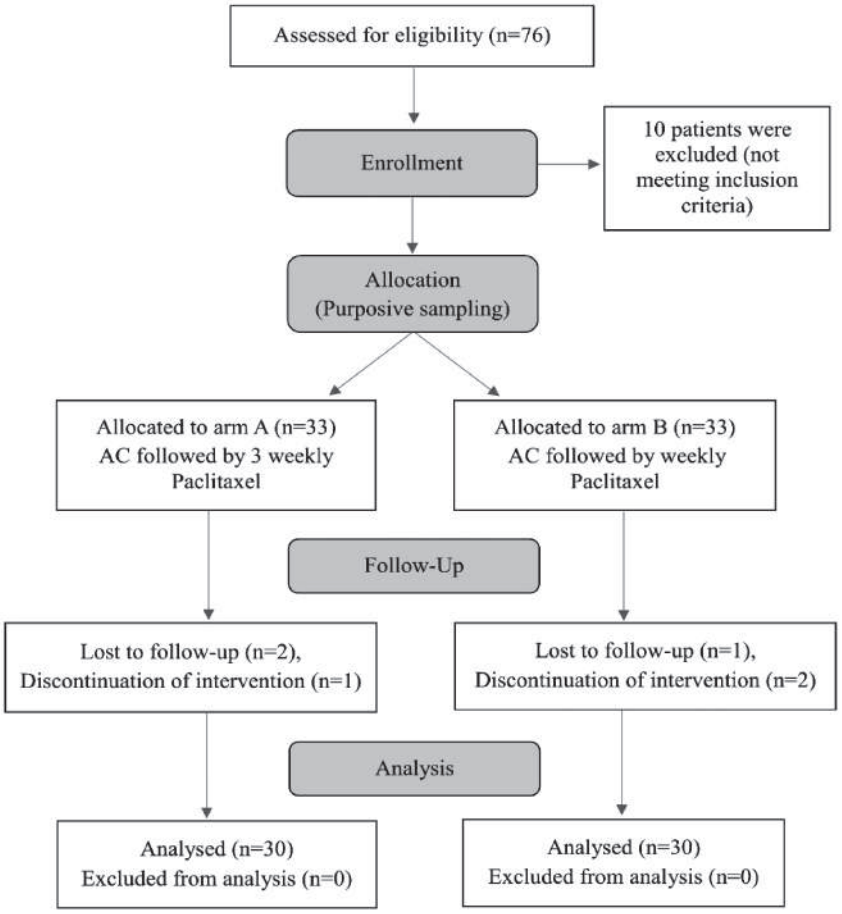


Figure 1: *Flowchart showing the methods of patient selection, allocation, follow-up and analysis*

Table 1: *Distribution of patients according to the baseline characteristics*

Variable	Arm A(n = 30)	Arm B(n = 30)	Total(n = 60)	p-value*
Age range (years)				
30-40	4 (13.33%)	5 (16.67)	9 (15)	
41-50	12 (40%)	15 (50)	27 (45)	
51-60	10 (33.34%)	9 (30)	19 (31.67)	0.513
61-70	4 (13.33%)	1 (3.33)	5 (8.33)	
ECOG performance status				
0	5 (16.66%)	2 (6.67)	7 (11.67)	
1	14 (46.67%)	18 (60.0)	32 (53.33)	0.4
2	11 (36.67%)	10 (33.33)	21 (35.0)	
Laterality of involved breast				
Left	18 (60%)	21 (70)	39 (65)	0.417
Right	12 (40%)	9 (30)	21 (35)	
Involved quadrant of breast				
Upper-outer	18 (60%)	20 (66.67)	38 (63.33)	
Upper-inner	3 (10%)	3 (10)	6 (10)	
Lower-inner	5 (16.67%)	5 (16.67)	10 (16.67)	0.99
Lower-outer	1 (3.33%)	0 (0.0)	1 (1.67)	
Central	3 (10%)	2 (6.66)	5 (8.33)	
Histology				
Ductal	24 (80%)	22 (73.33)	46 (76.67)	
Lobular	5 (16.67%)	6 (20)	11 (18.33)	0.774
Others	1 (3.33%)	2 (6.67)	3 (5)	
Histological differentiation (grade)				
Well	5 (16.67%)	4 (13.33)	9 (15)	
Moderate	9 (30%)	10 (33.34)	19 (31.67)	0.92
Poor	16 (53.33%)	16 (53.33)	32 (53.33)	
T stage (AJCC 8th edition)				
T1	0 (0%)	0 (0)	0 (0)	
T2	10 (33.33%)	9 (30)	19 (31.67)	
T3	15 (50%)	14 (46.67)	29 (48.37)	0.81
T4	5 (16.67%)	7 (23.33)	12 (20)	
N stage (AJCC 8th edition)				
N0	7 (23.33%)	6 (20)	13 (21.67)	
N1	15 (50%)	14 (46.67)	29 (48.33)	0.948
N2	7 (23.33%)	9 (30)	16 (26.67)	
N3	1 (3.34%)	1 (3.33)	2 (3.33)	
Stage group (AJCC 8th edition)				
IIIA	17 (56.67%)	19 (63.33)	36 (60)	
IIIB	9 (30%)	9 (30)	18 (30)	0.678
IIIC	4 (13.33%)	2 (6.67)	6 (10)	
Hormone receptor status of tumor				
ER and/or PR +ve	21 (70%)	23 (76.67)	44 (73.33)	0.559
ER and PR both -ve	9 (30%)	7 (23.33)	16 (26.67)	
Ki-67 Proliferation index				
>20%	21 (70%)	22 (73.33)	43 (71.67)	0.774
<20%	9 (30%)	8 (26.67)	17 (28.33)	

* Calculated using Student's t test or Chi-square (χ^2) test

ECOG = Eastern Cooperative Oncology Group, AJCC = American Joint Committee on Cancer, ER = estrogen receptor, PR = progesterone receptor

Table-2 compares the various acute hematological toxicities observed between the two arms from the start of the treatment up to its completion. Eighteen (60%) and 2 (06.67%) of patients developed grade 2 and 3 anemia in arm B, whereas 12 (40.60%) and 01 (03.34%) patients developed grade 2 and 3 anemia respectively in arm A. These findings were not statistically significant ($p > 0.05$). Leucopenia of various grades was predominant in both the Arms. Grade 2 or more leucopenia was seen in 22 patients (73.33%) vs 20 patients (66.66%) among arm A and B respectively. The finding was not statistically significant ($p>0.05$). Five (16.67%) patients in arm A and 2 (6.66%) in arm B developed febrile neutropenia. Thrombocytopenia was predominantly seen in arm A compared to arm B. Two (10.00%) patients in arm A developed grade 2 or more thrombocytopenia. The finding was not statistically significant ($p>0.05$).

Table-3 shows acute non-hematological (GIT-related) toxicities observed between the two arms from the start of the treatment up to the completion of the treatment. Overall, 32 (53.34%) and 30 (50.00%) patients had grade 1 nausea and vomiting respectively. None of the patients had grade 3 nausea and vomiting. Nearly two-third patients (73.33%) did not have any event of diarrhea.

Table 2: *Acute hematological toxicities during chemotherapy in both arms*

Hematological toxicities		Arm A(n = 30)	Arm B(n = 30)	Overall(n = 60)	p-value*
Anemia	Grade 0	0	0	0	0.187
	Grade 1	17 (56.66)	10 (33.33)	27 (45.00)	
	Grade 2	12 (40.00)	18 (60.00)	30 (50.00)	
	Grade 3	01 (03.34)	02 (06.67)	03 (05.00)	
Leucopenia	Grade 0	0	0	0	0.732
	Grade 1	08 (26.66)	10 (33.33)	18 (30.00)	
	Grade 2	16 (53.33)	16 (53.33)	32 (53.34)	
	Grade 3	06 (20.00)	04 (13.34)	10 (16.66)	
Thrombocyto-penia	Grade 0	18 (60.00)	21 (70.00)	39 (65.00)	0.43
	Grade 1	10 (33.33)	09 (30.00)	19 (31.67)	
	Grade 2	02 (6.67)	0	02 (03.33)	
	Grade 3	0	0	0	
Febrile neutropenia**	Grade 0	25 (83.33)	28 (93.33)	53 (88.33)	0.228
	Grade 3	05 (16.67)	02 (06.67)	07 (11.66)	

* Calculated using Chi-square (χ^2) test.

** There is no grade 1 or 2 for febrile neutropenia according to CTCAE version 5.0, Grade 0 = not present

Table 3: *Acute (GIT-related) toxicities observed during chemotherapy*

Toxicities		Arm A (n = 30)	Arm B (n = 30)	Overall (n = 60)	p-value*
Nausea	Grade 0	03 (10.00)	07 (23.33)	10 (16.66)	0.378
	Grade 1	17 (56.67)	15 (50.00)	32 (53.34)	
	Grade 2	10 (33.33)	08 (26.66)	18 (30.00)	
	Grade 3	0	0	0	
Vomiting	Grade 0	07 (23.33)	10 (33.33)	17 (28.33)	0.69
	Grade 1	16 (53.33)	14 (46.67)	30 (50.00)	
	Grade 2	07 (23.33)	06 (20.00)	13 (21.67)	
	Grade 3	0	0	0	
Diarrhea	Grade 0	19 (63.33)	25 (83.33)	44 (73.33)	0.327
	Grade 1	05 (16.67)	03 (10.00)	08 (13.33)	
	Grade 2	04 (13.33)	01 (03.34)	05 (08.33)	
	Grade 3	02 (06.67)	01 (03.34)	03 (05.55)	

* Calculated using Chi-square (χ^2) test

Table 4: *Other acute toxicities observed during chemotherapy*

Toxicities		Arm A(n = 30)	Arm B(n = 30)	Overall(n = 60)	p-value*
Neuropathy	Grade 0	06 (20.00%)	02 (06.67)	08 (13.33)	0.296
	Grade 1	15 (50.00%)	13 (43.33)	28 (46.67)	
	Grade 2	07 (23.33%)	11 (36.67)	18 (30.00)	
	Grade 3	02 (06.67%)	04 (13.33)	06 (10.00)	
Myalgia	Grade 0	04 (13.33%)	02 (06.67)	06 (10.00)	0.37
	Grade 1	06 (20.00%)	12 (40.00)	18 (30.00)	
	Grade 2	16 (53.34%)	13 (43.33)	29 (48.33)	
	Grade 3	04 (13.33%)	03 (10.00)	07 (11.67)	
Sinus bradycardia	Grade 0	21 (70.00%)	23 (76.67)	44 (73.33)	0.77
	Grade 1	08 (26.66%)	07 (23.33)	15 (25.00)	
	Grade 2	01 (03.34%)	0	01 (01.67)	
	Grade 3	0	0	0	
Alopecia	Grade 1	27 (90.00%)	25 (83.33)	52 (86.67)	0.45
	Grade 2	03 (10.00%)	05 (16.67)	08 (13.33)	
Nail changes	No	29 (96.66%)	28 (93.33)	57 (95.00)	0.553
	Yes	01 (03.34%)	02 (06.67)	03 (05.00)	

* Calculated using chi-square (χ^2) test or Fisher exact test

Table-4 shows various non-GIT, non-hematological toxicities in both arms during chemotherapy. Patients mostly had grade 1 toxicities. A few patients had grade 3 neuropathy (6 patients, 10%) and myalgia (7 patients, 11.67%) including both arms.

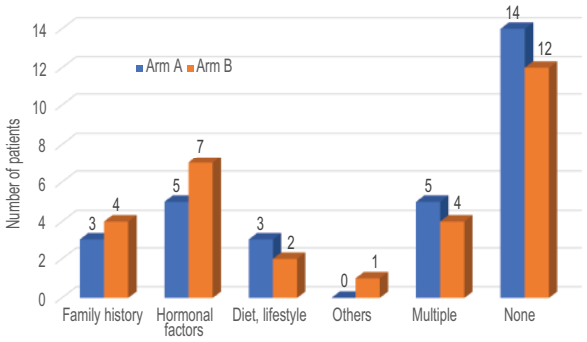


Figure 2: *Distribution of patients according to risk factors*

Discussion

Sixty patients with HER2-negative stage III breast cancer were analyzed for this study. All the patients were assessed for toxicity before starting the treatment as well as before each cycle of chemotherapy. Hematological toxicities like anemia, leucopenia and thrombocytopenia were common in both arms. None of the toxicities were statistically significant.

Acute hematological toxicities were observed between the two arms from the start of the treatment up to its completion. All of the patients had some degree of both anemia and leucopenia while most were spared from thrombocytopenia. Grade 1 anemia occurred in 56.66% and 33.33% of patients in arm A and arm B respectively. The severity of anemia was slightly higher in arm B compared to arm A. More patients in arm B had grade 2 (60% vs 40%) and grade 3 (6.67% vs 3.34%) anemia in comparison to arm A. The findings were not statistically significant (p 0.187).

Grade 2 leucopenia was found in 16 (53.33%) patients in both arms. Six patients from arm A (20%) and four patients from arm B (13.34%) developed grade 3 leucopenia. The finding was statistically not significant (p 0.732). Regarding thrombocytopenia, none of the patients from both arms had grade 3 toxicity during their treatment. Grade 1 and 2 was predominantly seen in arm A (33% and 10%) compared to Arm B. The findings were not statistically significant (p 0.43). But similar findings were reported by Untch et al[13].

Seidman et al. reported a very well tolerable toxicity profile of weekly paclitaxel[8]. They mentioned that none of their patients (30) had any event of febrile neutropenia. A similar finding was noted in the present study. More than 88% patients (53) had no events of febrile neutropenia. Seven (11.66%) patients had febrile neutropenia, which was predominantly found in arm A (5 or 16.66% patients).

Regarding non-hematological toxicities, a variety of toxicities were observed and analyzed between two arms. Nausea and vomiting were almost similar on both arms. Most of the patients had grade 1 nausea and vomiting. Overall, more than half of the patients (53.33%) had grade 1 nausea, whereas, 50% had grade 1 vomiting. The study findings had a range of variations regarding nausea and vomiting. Martin et al. reported 34% and Abu Khalaf et al. mentioned 24% incidence of nausea. [14,15] Palappallil et al. found almost 90% event of grade 1 nausea and vomiting in their study[16]. This wide range of variation is probably due to different patient factors and difference in antiemetic protocols among centers as well. A few patients had grade 2 toxicities (nausea 30% and vomiting 21.67%) in this study. The differences between the two arms were not statistically significant. Most patients (73.33%) did not have any event of diarrhea. But 3 patients (3.33%) developed grade 3 diarrhea. The observed differences between the two arms were not significant (p 0.327).

Grade 2 and 3 neuropathies were more commonly found in arm B (36.67% vs 23.33%, and 13.33% vs 6.67% respectively). However, arm B had lesser (43.33%) events of grade 1 toxicity than arm A (50.00%). These findings were not statistically significant between the two arms (p 0.296**)**. Untch et al. also mentioned higher grade 2 and 3 neurotoxicity (31% and 06% respectively) in dose dense arm whereas higher percentage of grade 1 toxicity in conventionally schedule of chemotherapy, which correlates with the present study[13].

Burtness et al. mentioned that increased dose of paclitaxel was associated with grade 3 toxicity of myalgia. [17] But this study showed some dissimilarity in this context. Overall, about half of the patients in both arms had grade 2 toxicity of myalgia. In arm A it was 53.34%, and 43.33% in arm B.

In this study, majority of the patients completed their treatment without any significant cardiotoxicity. Asymptomatic sinus bradycardia was the most commonly observed cardiac event and hence was analyzed. A little over 25% of patients developed sinus bradycardia and the distribution was nearly equal in both arms.

All the patients in both arms had some degree of alopecia. Both Kuraparthy et al. and Palappallil et al. mentioned about presence of alopecia in all the study population[16,18]. In our study, 86.67% of the patients had grade 1 alopecia in both arms. The differences between the arms were not significant (p 0.553).

It is noteworthy that none of the patient discontinued the treatment for adverse events of chemotherapy. In both arms, all patients completed their planned chemotherapy schedule. Toxicities were managed with conventional treatment and the patients were kept in close follow up subsequently.

Lack of randomization was the main limitation of this study. As it was a non-randomized study selection bias was present. The time period was short to evaluate late toxicities which exert important role on disease free survival or overall survival. Patients were sampled from two centers of Dhaka city. So, it doesn't reflect the nationwide scenario.

Conclusion

This study aimed to evaluate the toxicities of four cycles of three-weekly administrations of AC followed by paclitaxel weekly or every three weeks in neoadjuvant setting in HER2 negative, stage III breast cancer patients. The weekly schedule was found to be equally safe with manageble toxicity profile in comparison to the three-weekly schedule. However, the limitations of study necessitate further systematic evaluation.

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Contribution: Conceptualization: SB; Data curation & analysis: SB, MMR; Funding acquisition & investigation: SB, MMR, MAB, KS, ARS, SKT, MAH; Project administration & validation: SB, MMR, MAB; Writing – review & editing: SB, MMR, MAB

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Case Report

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Recurrent Retroperitoneal Liposarcoma with Colonic Involvement with an Unexpected Finding: A Case Report

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Abstract:

A 50-year-old male, previously diagnosed and operated upon as a case of retroperitoneal liposarcoma, presented with rapidly enlarging right sided abdominal mass. CT scan revealed a mixed density mass of about 24′7′8 cm and tru-cut biopsy confirmed lipsarcoma. At laparotomy, a textiloma was found just below and adhered to the peritoneum. The tumor infiltrated the right colon, which was dilated. En bloc excision of the mass along with right hemicolectomy was performed. Histopathology confirmed tumor infiltration into the colon. Recurrence of RPS is not uncommon and many incidences have been reported in literature. But concomitant findings of a retained surgical mop along with tumor in-growth inside the colon is rare. Here we present such a rare case with unexpected findings at laparotomy.

Key words: *retroperitoneal sarcoma, recurrent, textiloma*

Introduction:

Retroperitoneal sarcomas (RPS) are rare tumors comprising of 15% of all soft tissue sarcomas.[1] RPS typically have high local recurrence rate, despite excision with negative margins; and recurrences as late as 10 years have been seen in some cases.[2,3] Recurrent STS typically present with an abdominal lump and may be associated with pressure symptoms like intestinal obstruction. But direct colonic involvement of RPS is extremely rare.[4] Another rare

event is retained surgical sponge, simply known as 'textiloma'. It is estimated that retained surgical items occur in 1 in every 5500 to 18,760 inpatient operations but may be as high as 1 of every 1000 to 1500 abdominal cavity operations.[5,6] This may result in a broad spectrum of clinical presentations, and delayed presentations months, years, or, in some cases, decades later following the index surgical procedure have been reported.[7] Here we present such a case that harbored all these rare events in a single patient.

Case:

A 50-year-old male reported at surgical oncology OPD of NICRH with a rapidly enlarging right sided abdominal mass with features of subacute intestinal obstruction. He was a known case of retroperitoneal liposarcoma and underwent laparotomy and excision at the same hospital 6 years back (2018). He received no adjuvant treatment in the intervening period.

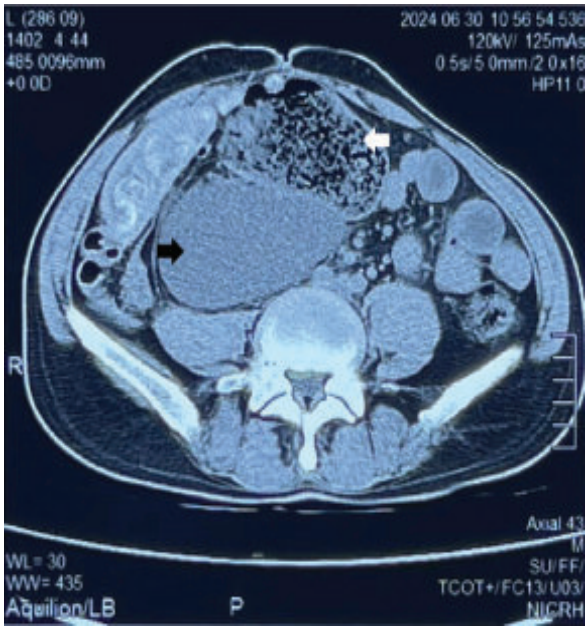


Figure 1: *Axial CT scan showing recurrent intraabdominal soft tissue mass (black arrow) with the textiloma just underneath the parietal wall (white arrow)*

Examination revealed a 20x15 cm firm, lobulated mass occupying right hypochondriac, right lumbar, umbilical, and right iliac region. The mass was fairly immobile. CECT of abdomen showed a mixed density mass having solid and cystic component (AP-8cm X TR-7 cm X CC-24 cm) in rt side of abdomen occupying epigastric, rt hypochondriac and rt side of umbilical region (Fig. 1). Mass displaced pancreas left laterally. Liver and both kidneys were normal. CT-guided tru-cut biopsy confirmed liposarcoma. The case was discussed in tumor board and decision of surgical exploration was taken.

At the day of surgery, a DJ stent was inserted in rt ureter as precautionary measure. Abdomen was opened through midline incision and a hard lump was found just below and adhered to the peritoneum with loops of bowel tethered to it. Careful examination revealed it was a textiloma made up of a skin mop of about 14X8 cm (Fig. 2). It was dissected free and removed separately. The retroperitoneal mass occupied most of the central and rt mid-to-lower abdomen. Cecum and ascending colon was found hugely dilated, about 8-10 cm, and the growth could not be separated from the colon. Right kidney, 2nd part of duodenum and pancreas was in close proximity of the tumor but there was no malignant infiltration. Major vessels were also not involved. An en bloc excision of the mass along with right hemicolectomy was performed. Patient was recovering well and oral feeding was commenced from 6th POD but on 8th POD bile was seen in the subhepatic drain tube. Reexploration was done but no leakage site could be identified. Ileocolic anastomosis was also intact. The subhepatic bile collection was cleared and abdomen was closed after peritoneal wash and with another drain kept in the pelvis. After that patient's recovery was smooth and uneventful and patient was discharged on 22nd POD of the initial laparotomy. Histopathology reported liposarcoma FNCLCC G1 (WD), Mitoses 2-3/10HPF. Intestinal resection margins were free. Immunohistochemistry showed MDM-2 focally positive. The patient is doing well at 8 months after surgery.

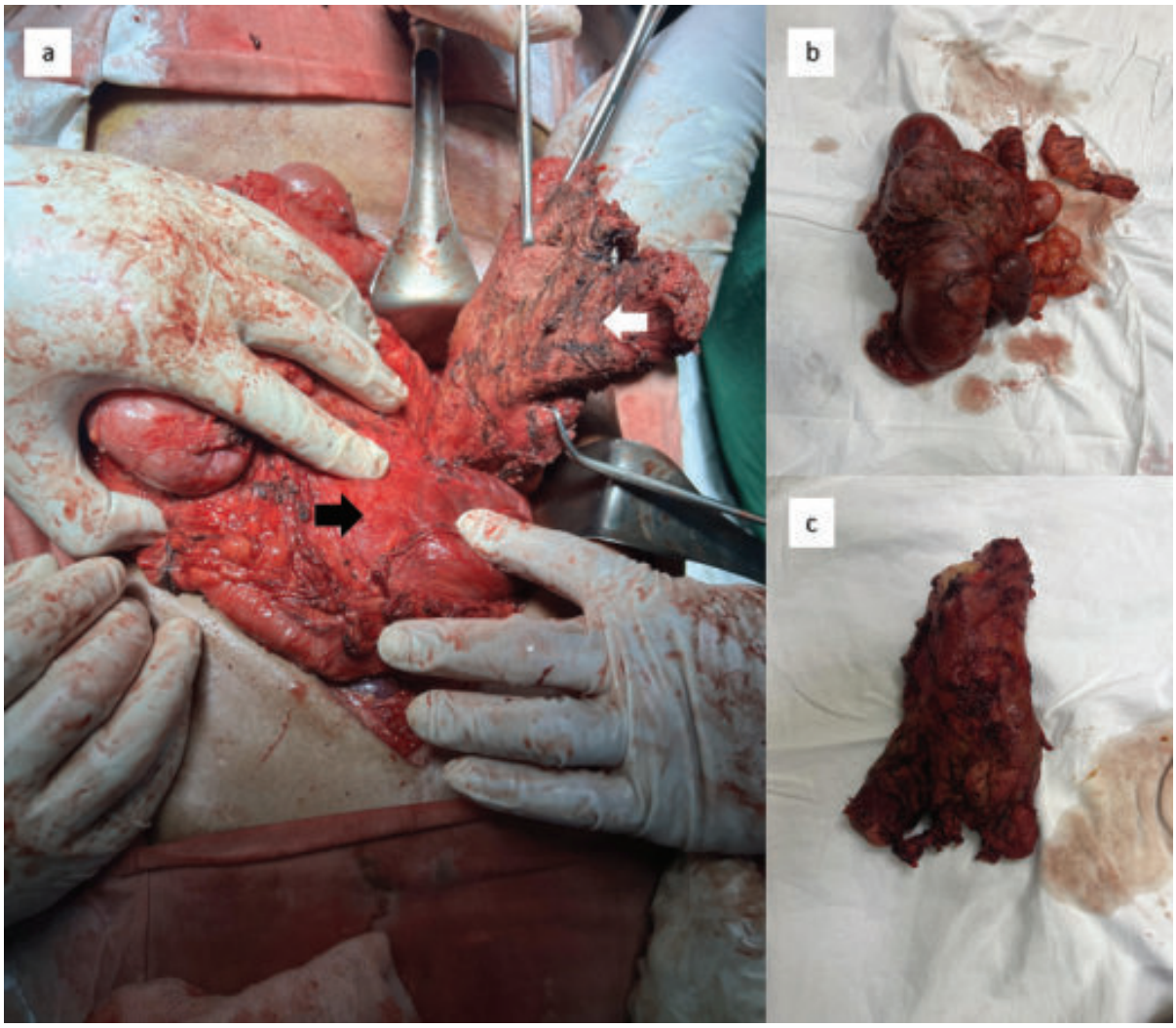


Figure 2: *Peroperative photos, (a) Textiloma (white arrow) is dissected free from the peritoneum above and the soft tissue mass below (black arrow), (b) Part of the excised retroperitoneal mass with bowel segment, (c) Textiloma*

Discussion:

Soft tissue sarcomas are uncommon tumors, representing merely 1% to 2% of all solid cancers. Of them, only 15% occur in retroperitoneum.[1] Patients may present with an asymptomatic abdominal mass or they may present with abdominal pain. Some might have pressure effects, including lower limb edema, referred pain, early satiety, bowel obstruction, or ascites. Distant metastases are present at the time of diagnosis in approximately 10 percent of patients, mainly in lung and liver.[8-12]

In adults, the most common histologic types of retroperitoneal soft tissue sarcomas are liposarcoma and leiomyosarcoma, followed by undifferentiated/ unclassified STS. Among the different variants of liposarcoma that present in the retroperitoneum, the most common are well-differentiated (low-grade) liposarcomas, followed by dedifferentiated liposarcomas. Myxoid, round cell, and pleomorphic liposarcomas are uncommonly found in the retroperitoneum.[13-16] Among children, the most common histologic types of retroperitoneal sarcomas (RPS) are extraskeletal Ewing sarcoma/primitive neuroectodermal tumor (PNET), alveolar rhabdomyosarcoma, and fibrosarcoma.[17]

Tumor staging is done using the 8th edition of the AJCC/UICC staging system which has separate T staging classification and prognostic stage grouping for RPS. For patients with localized resectable primary RPS, surgery with macroscopic complete resection provides the only opportunity for cure. R1 resections are accepted as a form of complete resection because R0 resections, while ideal, are rarely achieved due to the large size and anatomic complexity of these tumors.[18] Most patients with RPS are put under surveillance only after a complete macroscopic (ie, R0/R1) resection. Management of patients with gross residual disease after surgery is complex, options include re-resection or surveillance, with adjuvant RT discouraged due to lack of evidence of clinical benefit.[19,20]

RPS typically have high rate of recurrence, mostly local. Well-differentiated liposarcoma has the most favorable prognosis, but it also has the highest rates of local recurrence, along with its dedifferentiated variety. Recurrence may occur as late as ten years or more in some patients.[2,3]

Each case of recurrent RPS is unique and care must be individualized. For an isolated local recurrence, resection should be attempted if feasible. Approximately 60% of such tumors are potentially resectable, and five-year survival rates after reresection may be as high as 50%.[21] Patients with longer time to recurrence, low-grade tumors and no history of tumor rupture at surgery are most likely to benefit from resection. Patients who did not receive any RT as part of their primary treatment, may benefit from preoperative RT. Intraoperative RT is also an option. In case of unresectable recuerrences, role of debulking surgery is unclear. Repeated surgical debulking may be a reasonable option for some patients with low-grade (ie, well-differentiated) liposarcomas.[22]

Our patient was disease free for almost 6 years after initial surgery. When he presented with an intraabdominal mass again, he was clinically diagnosed as a case of local recurrence. CECT abdomen confirmed this, with radiologist reporting a “mixed density mass lesion with solid and cystic component”. Needle biopsy also reported as liposarcoma. But during laparotomy, there were two surprises waiting for the surgical team. One was the surgical mop (known in literature as textiloma or gossipybioma) that was found just below the parietal wall. The other was tumor ingrowth inside the bowel lumen casing marked dilataion of the ascending colon. That two relatively rare phenomena occurred in the same patient is truly extraordinary.

Unintended retention of a foreign object (URFO) is a broad term used to define any item left in a patient at the time of a procedure. Surgical sponges are the most common retained item compared with other items used in surgery. The problem of retained surgical sponge is known as “gossypiboma”, and also as “textiloma”, “gauzoma”, or “muslinoma”.[23,24] It is estimated that retained surgical items occur in 1 in every 5500 to 18,760 inpatient operations but may be as high as 1 of every 1000 to 1500 abdominal cavity operations.[25,26] Retained surgical sponge results in a broad spectrum of clinical presentations. Reported time to diagnosis is 1 day to 40 years.[27,28] In general, two distinct clinical patterns of retained surgical sponge are described: exudative and fibrinous. The early or exudative pattern presents in the postoperative period as a result of local inflammation as a response to the foreign body. The immediate presentation is surgical site infection in the form of wound dehiscence, abscess, fistula formation, or sepsis. Other clinical presentations involve extrusion of the sponge, which can occur externally through the wound or by fistulization into the rectum, vagina, or bladder. Sponge erosion and migration internally can lead to intestinal obstruction, malabsorption, or gastrointestinal hemorrhage.[29] A fibrinous pattern refers to the encapsulation of the retained foreign object within scar tissue, which presents in a delayed fashion (>60 days) representing approximately 25 percent of all cases. Delayed presentations months, years, or, in some cases, decades later following the index surgical procedure have been reported.[30] The fibrinous clinical pattern presents as a soft tissue mass in approximately 27% of patients[31], or as an aseptic foreign body granuloma with adhesions and encapsulation with “pseudotumor” formation. Some may mimic carcinoma, leading to ill-advised attempts at biopsy or radical excision of involved organs en bloc.

Computed tomography (CT) scan is superior to other imaging modalities for evaluating the source of symptoms and detecting retained intraabdominal surgical sponge.[32] The most characteristic appearance of retained sponge is a low-density heterogeneous mass with a spongiform pattern that contains gas bubbles.[32]

Retroperitoneal liposarcoma with colonic involvement is very rare, with only three reported cases in English

literature so far (Table 1).[4] Two of them were asymptomatic while one presented with melena.

So, this is a case of multiple rare events where patient remained asymptomatic with a retained mop for 6 years, Colonic tumor ingrowth also remained unnoticed. Only when the tumor became large, patient sought medical help. On evaluation, the textiloma was missed on CT scan as the tumor recurrence was the more obvious finding. But on retrospective analysis, the textiloma can be seen as a mass with separate density from the tumor and just under the parietal wall (Fig. 1). It probably would have gone unnoticed for longer time if the tumor had not recurred, prompting the patient to seek medical help. During laparotomy, the surgical team was taken by surprise by both the textiloma and the colonic involvement, proving once again that the abdominal cavity is truly a pandora's box.

Conclusion:

Recurrence of RPS is not uncommon and many incidences have been reported in literature. But concomitant finding of a retained surgical mop along with tumor in-growth inside the colon in a recurrent RPS patient is unheard of. This case can act as a reminder that RPS patients need lifelong surveillance even after complete excision. Multi-organ involvement is rare, but may occur and thorough evaluation including high resolution imaging is essential before embarking on surgery. Finally, strict operating room protocols should be adhered to at all times to avoid unwanted complications like retained surgical sponge.

Conflict-of-interest declaration

There is no potential conflict of interest.

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Case Report

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A Recurrent Case of Ocular Surface Squamous Neoplasia (OSSN) Treated with Electron Beam Radiotherapy Alone

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Abstract

The rise of electron beam radiotherapy represents growing recognition of its role in managing Ocular Surface Squamous Neoplasia (OSSN), which can help prevent vision and organ loss caused by enucleation. At present, there is no consensus or established guideline on the optimal management of OSSN.

This case study reports the use of electron beam radiotherapy in a patient with recurrent squamous cell carcinoma (SCC) of the left lower lid conjunctiva. Informed consent was obtained. The patient had previously undergone surgical excision with adequate negative margins. After one year, the disease recurred and was treated with topical chemotherapy; however, the disease progressed. She was subsequently treated with 50 Gy in 25 fractions of electron beam radiotherapy (15 MeV electrons), which resulted in complete disease regression.

At the end of six months of follow-up, the patient remained disease-free, with preserved visual acuity of 25/25. She experienced mild dry eye, which was well managed with topical lubricants. Long-term studies are recommended to further assess the impact of radiation on such cases.

Key words *Ocular Surface Squamous Neoplasia, Electron beam radiotherapy.*

Introduction

A SCC of the conjunctiva potentially life-threatening diagnosis as it can invade local structures more rapidly or form distant metastasis[1]. There are a number of treatment options accessible, for this condition. However, they all reveal high rates of recurrence[2]. There is inadequate clinical evidence to support one treatment alternative over another. The most common intervention used to treat SCC of the conjunctiva is Surgical excision. The eye is removed surgically via a technique called enucleation. This will reduce patients' quality of life and significantly influence their visual function[3]. For that reason, the development of a more cosmetically suitable reservation of ocular function electron beam radiotherapy is effective treatment for recurrent SCC of the conjunctiva. It would be favorable for patients diagnosed with this condition.

Case Report

A 67-year-old female presented with recurrent SCC of the left lower lid conjunctiva. Initially, the diagnosis was left lower lid meibomian gland carcinoma. That time the lesion was surgically removed by local excision and frozen section biopsy was done. The lesion again reappeared after 1-year of post-surgery and was consequently treated with Mitomycin C for about 2 weeks. At this time, pathology revealed Ocular Surface Squamous Neoplasia with high grade dysplasia. On treatment of topical chemotherapy disease was progress. Radiological findings of CT scan orbit revealed residual /recurrent subconjunctival thin, soft tissue mass 1 cm at lateral aspect of left eyeball without evidence of intraconal lesion (Figure 1).

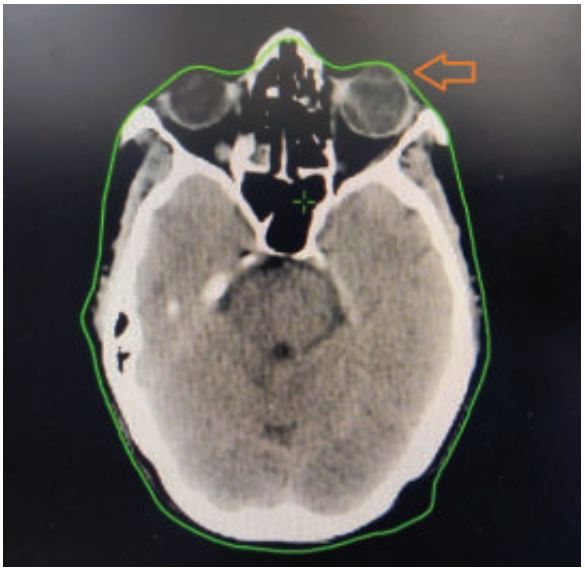


Figure 1: *CT scan of Orbits indicates subconjunctival soft tissue mass*

On examination, her visual acuity in the left eye was 25/25. Rest of the ocular examination was unremarkable. There was no regional lymphadenopathy. Considering her age and good vision in her left eye, exenteration was deferred. Successively, multidisciplinary consultation was taken and offered electron beam as another treatment preference for conservation of eye and vision. Then patient was treated with 15 MeV electrons external beam radiotherapy with linear accelerator to reach a cumulative dose of 50 Gy in 25 fractions over 5 weeks to the left eye. Radiation was given to the left lower lid conjunctiva with 1 cm margin beyond the orbital rim using custom made lead cut out defining the field of radiation and corneal shielding. The treated field size was 5x 3 cm, depth was 2.5 cm (Figure 2)

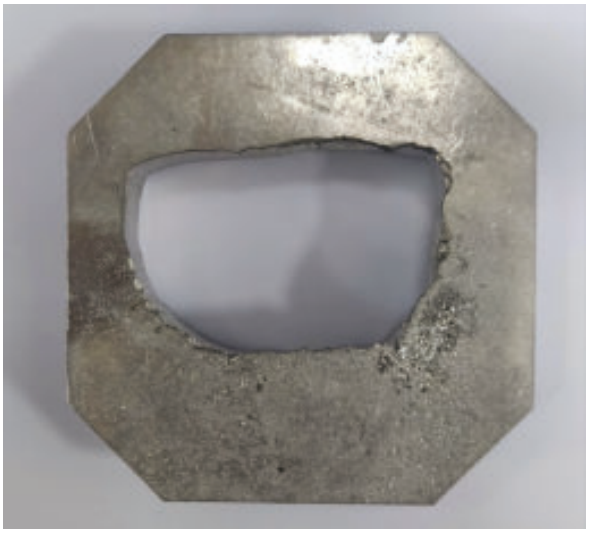


Figure 2: *Electron cutout used for radiotherapy*

Lubricating eye drops were prescribed for use prior to treatment administration to preclude drying of the ocular surface. During treatment, there were mild acute conjunctivitis which were self-limiting and diminished within 3 weeks of treatment. At 6 months post-treatment follow-up revealed disease control of patients also provides a unique case to suggest electron beam as a feasible opportunity for the treatment of recurrent OSCC. Furthermore, in this instance, vision was not compromised whereas delivering an excellent cosmetic outcome.

Discussion

The advantage of radiotherapy is to treat recurrent SCC of the conjunctiva by providing tumor control and preserving visual function with minimal side effects. When treating ocular neoplasia, radiotherapy facilitates ocular function preservation and improved cosmesis compared to the surgical removal of the eye by enucleation, that leaves the patient with one functional eye and monocular vision. In case of residual disease adjuvant, topical chemotherapy like mitomycin C, 5-fluorouracil, is prescribed[4].Topical chemotherapy causes long-term toxicity to the epithelium. There is no decisive guideline in literature precisely advantage of one adjuvant modality versus another like

chemotherapy, or radiotherapy. Nevertheless, exenteration remains conventionally recognized treatment in case of extensive OSSN. This leads to removal of eye with loss of vision and intense psychosocial implications due to the disfigurement and loss of self-esteem, and this may not always be amenable to rehabilitation easily by prosthesis. Radiation as an adjuvant treatment after surgery has been described in various forms for OSSN, which includes protons, brachytherapy, and stereotactic radiotherapy[5]. However, regarding protons therapy the cost effectiveness, the non-availability and long-term outcome data in routine practice still remain a significant limitation[6]. In cases restricted to the ocular coats, especially when there is residual scleral disease after primary excision, brachytherapy can be an excellent alternative[7]. Conversely, in the current case, the tumor involved the left lower eye lid. Hence, brachytherapy would not have been a suitable option for the current case. Radiotherapy could provide an alternative for the treatment of SCC of the conjunctiva, resulting in improved functional and cosmetic outcome. The electrons are special particulate types of radiation which devoid of much damage to surrounding tissues and deliver high dose of ionizing radiation to the tumor. Unlike photons, the electrons exit dose beyond the tumor, will have very insignificant radiation dose and so toxicities to the other eye and brain behind the treated eye are evaded[8]. These are benefits related to those predictable with the use of electrons often sparing lens and posterior eye structures. Frequently sparing lens and posterior eye structures photon radiation delivers more three-dimensional conformal dose than electrons. However, photon always has exit dose to consider that would cause more damage to the contralateral eye and brain (normal structure). External radiotherapy using electrons is an effective treatment option for invasive orbital OSSN. Inherent capacity of electron has no exit dose with treating surface. Hence, in cases such as these, electrons far better over photon radiotherapy by escaping the collateral impairment of eye that would have been affected by exit dose. While providing tremendous disease control and cosmesis It aids to reservation the eye and vision. Besides, electron radiotherapy is more widely available and inexpensive. Therefore, electron therapy may be equivalent to photon beam therapy in superficial tumors such as OSSN and has an advantage of low cost and wider accessibility devoid of conceding outcomes. While for all superficial tumors electrons have been used conventionally, and appropriate long-term data is accessible regarding dosimetry and safety. The acute toxicities of radiotherapy using electrons are least. The dry eye was merely acute toxicity seen in this patient, which is being efficiently managed with tear substitution only. Though, long-term studies involving larger numbers of patients are commended to aspect into the toxicities, effectiveness and profile in factor[9-11]. In this case, 6 months post-treatment demonstrates a noninferior approach compared to previous interventions with better cosmesis. As the ocular function of the left eye was conserved and visual acuity unaffected, this may have a supportive effect on patient quality of life in contrast to other treatments for recurrent SCC of the conjunctiva, and while in this study no measurement of quality of life was executed. Dry eye was the only reported side effect from treatment and is a common long-term ocular side effect from radiotherapy treatment. In this case, ocular lubricants were prescribed to manage symptoms of dryness and observed at follow-up appointments. Dry eye was self-reported. No grading scales are used for pre- or post-treatment dry eye. This was an inadequacy in this case study that may be included in advance studies considering electron beam radiotherapy for SCC of the conjunctiva.

Conclusion

This case study offers a snapshot of the role electron beam radiotherapy may play as an effective treatment option for recurrent SCC of the lower lid conjunctiva. Further studies, involving a larger patient cohort, are needed to better evaluate the role of electron beam therapy as an alternative and less invasive treatment for OSSN.

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Review Article

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The Role of PET-CT in Oncology

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Abstract

Positron Emission Tomography-Computed Tomography (PET-CT) has revolutionized oncology by providing high-resolution functional and anatomical imaging in a single scan. This hybrid imaging modality combines the metabolic information from PET with detailed structural data from CT, enhancing diagnostic accuracy, staging, treatment planning, and response assessment in various cancers. This review explores the principles, clinical applications, advantages, limitations, and future perspectives of PET-CT in oncology.

Keywords: *Cancer, PET, CT, ^{18}FDG, Standardized uptake value (SUV).*

Introduction

Cancer remains one of the leading causes of morbidity and mortality worldwide. In 2022, nearly 20 million new cancer cases were diagnosed, and approximately 9.7 million people died from the disease.[1] Among all sexes combined, the most commonly diagnosed cancers were lung (≈2.5 million cases, ~12.4% of all cancers), female breast (~11.6%), colorectal (~9.6%), prostate (~7.3%), and stomach (~4.9%). Lung cancer also accounted for the highest number of cancer-related deaths (≈1.8 million deaths, ~18.7%), followed by colorectal (~9.3%), liver (~7.8%), female breast (~6.9%), and stomach (~6.8%) cancers.[1]

Data on cancer incidence among children and adolescents (ages 0–19) are comparatively limited. According to the International Agency for Research on Cancer (IARC), approximately 275,000 new cases occur annually in this age group worldwide. However, more recent estimates suggest that the true burden may be higher, with roughly 400,000 children and adolescents (0–19 years) diagnosed with cancer each year.[2]

Accurate detection, staging, and disease monitoring are essential for improving patient outcomes. Imaging plays a central role in oncology, and the introduction of PET-CT has significantly transformed cancer management. By combining functional information from positron emission tomography (PET) with the anatomical detail of computed tomography (CT), PET-CT enables precise localization and characterization of lesions, enhancing clinical decision-making.[3]

Principles of PET-CT

PET imaging detects gamma rays emitted by positron-emitting radiotracers (e.g., ^{18}FDG). Provides metabolic information by highlighting areas of increased glucose uptake. CT imaging offers high-resolution anatomical details. Facilitates precise localization of PET findings. Hybrid PET-CT combines functional (PET) and structural (CT) imaging. Improves diagnostic confidence and reduces false positives/negatives.

Principles of PET-CT Imaging in Oncology

PET-CT integrates functional and anatomical imaging to provide a comprehensive evaluation of disease extent and metabolic activity. PET is based on the detection of gamma photons generated by the annihilation of positrons emitted from radiolabeled tracers, most commonly ^{18}F-fluorodeoxyglucose (^{18}F-FDG). Following administration, ^{18}F-FDG is taken up by metabolically active cells and phosphorylated, becoming trapped (because it can be neither metabolized further nor stored as glycogen) within tissues in proportion to glucose utilization. Malignant cells, characterized by increased glycolytic activity, therefore demonstrate higher radiotracer uptake, which can be quantitatively expressed using standardized uptake values (SUVs).[3] The CT component provides high-resolution anatomical information, allowing accurate localization of metabolic abnormalities, attenuation correction of PET data, and differentiation between physiological and pathological uptake. When combined, PET-CT produces fused images that align metabolic activity with structural detail, thereby enhancing lesion detection and characterization.[4]

Clinical Applications of PET-CT in Oncology

PET-CT has become an integral tool in oncologic management, providing both functional and anatomical information that guides diagnosis, treatment planning, and follow-up. In treatment planning, PET-CT allows precise delineation of metabolic tumor volumes (MTV) for radiotherapy, optimizing target coverage while sparing healthy tissue. It also aids surgical decision-making by distinguishing resectable from non-resectable disease, particularly in anatomically complex regions or in cases with suspected metastatic involvement.

Beyond planning, PET-CT is instrumental in assessing treatment response. By detecting changes in metabolic activity, it can identify responders and non-responders earlier than conventional imaging. This is especially relevant in lymphoma and esophageal cancer, where reductions in radiotracer uptake often precede measurable tumor shrinkage. PET-CT also helps differentiate residual viable tumor from post-therapy fibrosis or necrosis, thereby improving post-treatment evaluation.

In detection of recurrence, PET-CT demonstrates high sensitivity, identifying recurrent disease even when conventional imaging is inconclusive. It is particularly valuable when tumor markers rise without corresponding anatomical findings, such as in breast, head and neck, and colorectal cancers.[5]

While ^{18}F-FDG remains the most widely used tracer, emerging radiotracers are expanding PET-CT's clinical utility. ^{68}Ga-PSMA targets prostate-specific membrane antigen for prostate cancer evaluation, whereas tracers like ^{18}F-FLT and ^{18}F-FMISO provide insights into tumor proliferation and hypoxia, respectively, offering more tailored assessments of tumor biology and therapeutic response.[6,7]

Advantages of PET-CT

High Sensitivity & Specificity: Superior to standalone CT or MRI in many cancers.

Whole-Body Imaging: Detects distant metastases in a single scan.

Early Detection: Identifies metabolic changes before structural alterations.

How PET Differentiates Between Benign and Malignant Neoplasms:

Metabolic Activity: FDG Avidity (SUVmax): The most common PETradiotracer,^{18}F-Fluorodeoxyglucose (^{18}F-FDG), is a glucose analog taken up by cells with high metabolic demand. Malignant Tumors show Increased FDG uptake (hypermetabolic): Cancer cells exhibit Warburg effect—preferentially use glycolysis even in aerobic conditions[8]. Higher Standardized Uptake Value (SUVmax) typically indicates malignancy (e.g., SUVmax>2.5 is often suspicious).

Heterogeneous uptake: Aggressive tumors show irregular metabolic patterns.

Benign Lesions: Low or moderate FDG uptake (hypometabolic): Inflammatory or infectious processes (e.g., granulomas, tuberculosis) may show uptake but often with different patterns. Some benign tumors (e.g., adenomas) have minimal FDG avidity.

Time-Activity Curves (Dual-Time-Point Imaging): Malignant lesions often show increasing FDG uptake over time (e.g., at 1 hr. vs. 2 hr. post-injection). Benign lesions may show stable or decreasing uptake.[9]

Morphological Features in PET-CT Fusion: While PET assesses metabolism, CT provides anatomical details, improving specificity: Malignant Features on CT are irregular margins, necrosis, spiculated appearance (e.g., in lung cancer), invasion into adjacent structures & enlarged lymph nodes with high FDG uptake.

Benign Features on CT: Smooth margins, calcifications (e.g., in benign pulmonary nodules) & Fat density (e.g., lipomas).

Specific PET Tracers Beyond FDG: Some tumors have unique receptors/enzymes targeted by specialized tracers: ^{68}Ga-DOTATATE: For neuroendocrine tumors (NETs)[10]. ^{68}Ga-PSMA: For prostate cancer & ^{18}F-FLT (Fluorothymidine**):** Measures cell proliferation (more specific than FDG).[11,12]

SUV Thresholds in PET-CT: Differentiating Benign from Malignant Lesions.

The Standardized Uptake Value (SUV) is a semi-quantitative measure used in PET-CT to assess the metabolic activity of lesions. While no single SUV threshold can definitively distinguish benign from malignant lesions, certain ranges help guide clinical interpretation.

SUV Calculated as: Tissue radioactivity concentration (MBq/g)**) / Injected dose** (MBq/g) **/ Patient weight**(g)**.**

SUVmax = Highest SUV within a lesion (most commonly used).

SUVmean = Average SUV within a region of interest (ROI).

General SUV Thresholds for Malignancy. The "optimal" cutoff value for SUVmax can vary depending on the type of cancer being investigated, the specific imaging protocol, and the body part being examined. SUVmax <2.0 Likely benign, common in inflammation, fibrosis, or low-grade tumors. SUVmax 2.0–2.5 is interpreted as indeterminate. May require further evaluation (biopsy, follow-up). SUVmax >2.5 is suspicious for malignancy & often used as a cutoff in lung nodules, lymphoma. An SUV value between 2.5 and 5 is a finding that warrants caution and further investigation, such as a biopsy, clinical observation, or correlation with other imaging modalities, to determine the exact nature of the lesion. It is not definitively "normal" or "abnormal" on its own. SUVmax > 5.0–10.0 is highly suggestive of malignancy & aggressive cancers (e.g., small cell lung cancer, melanoma, esophageal cancer, metastatic disease).

Exceptions: Low-grade malignancies (e.g., well-differentiated neuroendocrine tumors) may have SUVmax<2.5.

Organ-Specific SUV Thresholds:

Lung Nodules: SUVmax>2.5: Suspicious for malignancy (sensitivity ~90%, specificity ~75%). SUVmax<1.5: Likely benign (but some adenocarcinomas may have low FDG uptake). False positives: Granulomas, infections (TB, histoplasmosis).

Lymphoma: SUVmax>4–5: Suggests aggressive lymphoma (e.g., DLBCL, Hodgkin's).

SUVmax<2.5: More common in indolent lymphomas (e.g., follicular lymphoma).

Head & Neck Cancers: SUVmax>3.5–4.0: Highly suspicious for malignancy. Physiological uptake (salivary glands, tonsils) can mimic disease.

Colorectal Cancer: Primary tumors: Typically, SUVmax>5–8. Liver metastases: Often SUVmax>3.5.

Breast Cancer: Invasive ductal carcinoma: SUVmax>2.5–3.0. Lobular carcinoma: Often have lower FDG uptake (maybe missed).

Prostate Cancer: FDG-PET has limited sensitivity (low uptake in many cases).

^{68}Ga-PSMA PET is preferred (PSMA SUVmax>5 suggests malignancy).

PET-CT has become an essential imaging modality in oncology due to its high sensitivity and specificity, often surpassing standalone CT or MRI in detecting various cancers. It allows whole-body imaging in a single session, facilitating the identification of distant metastases, and can detect early metabolic changes before structural alterations become apparent. PET differentiates benign from malignant lesions primarily through metabolic activity, with 18F-Fluoro-deoxyglucose (FDG) uptake serving as the most common indicator. Malignant tumors typically exhibit increased FDG uptake (hypermetabolic) due to the Warburg effect, often showing heterogeneous patterns

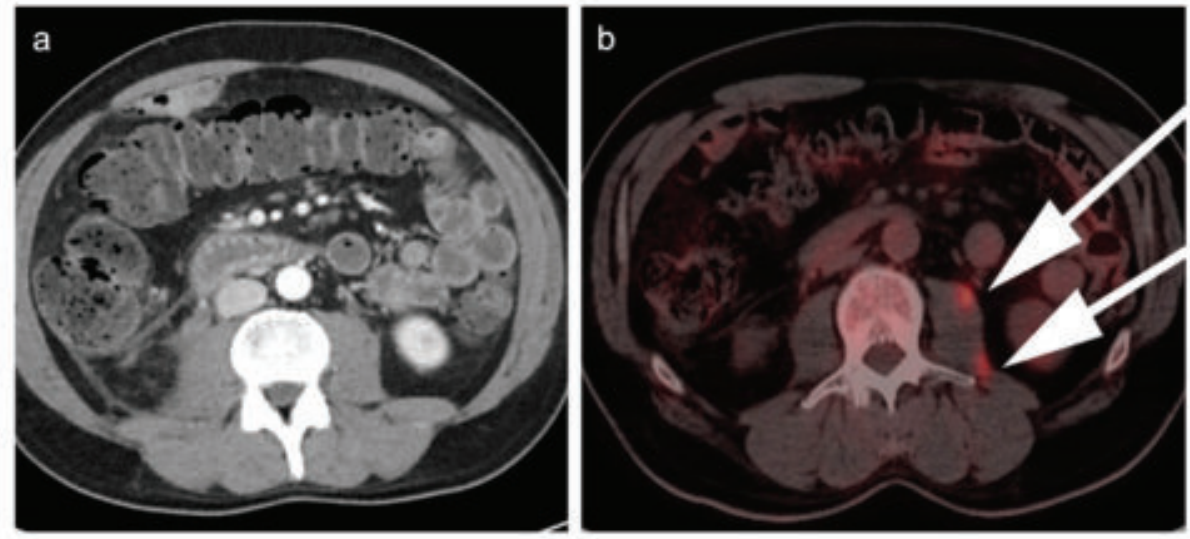


Figure 1. A 50-year-old-male with diagnosis of follicular lymphoma (FL) within an excised lymph node of the neck underwent baseline staging. (a) Axial contrast enhanced computed tomography (CT) image shows no disease in the abdomen.; (b) Axial fused [^{18}F] fluorodeoxyglucose positron emission tomography-CT (FDG PET-CT) images, show two hypermetabolic sites of subsequently biopsy-proven FL in the left psoas muscle (white arrows). FDG PET-CT upstages disease in 19% of patients with FL, revealing occult sites not seen on other conventional imaging.

and higher standardized uptake values (SUVmax), whereas benign lesions generally display low or moderate uptake, though inflammatory or infectious processes may produce variable patterns. Dual-time-point imaging can further aid differentiation, as malignant lesions often demonstrate increasing uptake over time, while benign lesions tend to remain stable or decrease. PET-CT fusion adds anatomical context, with malignant features on CT including irregular margins, necrosis, spiculated appearance, invasion into adjacent structures, and enlarged FDG-avid lymph nodes, whereas benign lesions usually have smooth margins, calcifications, or fat density. Beyond FDG, specialized PET tracers such as ^{68}Ga-DOTATATE for neuroendocrine tumors, ^{68}Ga-PSMA for prostate cancer, and 18F-FLT for proliferative activity enhance diagnostic specificity. The SUV, a semi-quantitative measure of lesion metabolic activity, assists clinical interpretation, with thresholds guiding malignancy suspicion across organ systems, although exceptions exist, including low-grade malignancies with low SUVmax or highly aggressive tumors with very high SUVmax. Organ-specific SUV ranges further refine assessment, such as SUVmax>2.5 in lung nodules suggesting malignancy, SUVmax>4–5 in aggressive lymphomas, and PSMA SUVmax>5 in prostate cancer, while physiological uptake and inflammatory processes must be considered to avoid false positives.[13]

Limitations and Challenges of PET-CT in Oncology

Despite its clinical utility, PET-CT has inherent limitations that can affect diagnostic accuracy. False-positive findings may occur due to increased radiotracer uptake in benign conditions such as infections (e.g., tuberculosis, fungal infections), inflammatory disorders (e.g., sarcoidosis, rheumatoid arthritis), or physiological uptake in brown fat and active muscles. Conversely, false-negative results can arise in malignancies with inherently low FDG uptake, including low-grade tumors (e.g., well-differentiated neuroendocrine tumors), small lesions below the PET spatial resolution (<5–8 mm), and certain tumor types such as renal cell carcinoma and mucinous adenocarcinoma. Additional challenges include high cost and limited availability, which can restrict widespread clinical adoption, and radiation exposure, as patients receive ionizing radiation from both PET and CT components.

Future Perspectives

Advances in imaging technology and computational methods are poised to address current limitations. Artificial intelligence (AI) shows promise in improving

image interpretation, lesion detection, and tumor segmentation. The development of novel radiotracers targeting specific tumor characteristics is expanding PET-CT's role in personalized oncology. Furthermore, PET-MRI is emerging as a complementary modality, offering high soft-tissue contrast while reducing radiation exposure, potentially improving lesion detection in selected tumor types.

Conclusion

PET-CT has revolutionized oncologic imaging by integrating metabolic and anatomical information, facilitating accurate diagnosis, staging, treatment planning, and response assessment. While limitations such as false positives, false negatives, radiation exposure, and accessibility remain, ongoing advancements in novel radiotracers, hybrid imaging techniques, and artificial intelligence are poised to further enhance its precision and clinical utility. PET-CT continues to play a central role in personalized cancer management, supporting more informed therapeutic decisions and improved patient outcomes.

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Erratum

Advanced Intraocular Retinoblastoma: A Review of Current Management Practices in Developing Countries

In the article "Advanced Intraocular Retinoblastoma: A Review of Current Management Practices in Developing Countries" published in Cancer J Bangladesh. Vol. 5, No. 2: July 2024, an error occurred in Figure 1. The figure was inadvertently printed incorrectly.

The correct Figure 1, illustrating the classification boundaries of advanced intraocular RB (Group D & E) by the International Intraocular Retinoblastoma classification & the International Classification of Retinoblastoma system is provided below:

<table>
<tr><td>IIRC</td><td colspan="2">Group D</td><td>Group E</td></tr>
<tr><td>ICRB</td><td>Group D</td><td colspan="2">Group E</td></tr>
</table>

Fig. 1: Showing classification boundaries of advanced intraocular RB (Group D & E) by the International Intraocular Retinoblastoma classification & the International Classification of Retinoblastoma system (Modified from Sedaghat et al. Canadian Journal of Ophthalmology 2024;59(5): e635-e641)

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