ORIGINAL ARTICLE

Perioperative FLOT Chemotherapy in Resectable Gastric Adenocarcinoma: A Single-center Retrospective Observational Study

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Abstract

Introduction: Gastric cancer (GC) is a leading cause of cancer-related mortality worldwide. Perioperative chemotherapy improves tumor downstaging and survival rates. The FLOT regimen was proven superior in the FLOT4-AIO trial, establishing it as the standard care for resectable gastric adenocarcinoma. Despite these encouraging results from randomized controlled trials, real-world data on the feasibility and outcomes of FLOT in diverse patient populations, particularly in low- and middle-income settings, remain limited. This study aimed to assess the feasibility, safety, and clinical outcomes of perioperative FLOT chemotherapy in patients with resectable gastric adenocarcinoma at a tertiary care center.

Materials and methods: We conducted a retrospective review of the medical records of patients diagnosed with resectable gastric adenocarcinoma who received perioperative FLOT chemotherapy between April 2019 and April 2025. The primary outcomes were the feasibility of perioperative FLOT chemotherapy and pathological complete response (pCR). The secondary outcomes were surgical outcomes, treatment adherence, and adverse events (AEs).

Results: The results showed that 64.4% of patients completed at least four cycles of neoadjuvant FLOT, while only 24.4% underwent surgical resection. No pathological complete responses were observed. Grade 3–4 AEs occurred in 18.1% of patients, primarily cytopenias. A high rate of loss to follow-up (45.4%) was noted in the preoperative phase.

Conclusion: While FLOT demonstrated an acceptable safety profile, the lower-than-expected surgical resection rate and high attrition highlight the challenges in managing locally advanced gastric cancer in real-world settings. This study emphasizes the need for strategies to improve treatment adherence and optimize patient selection to maximize the benefits of perioperative chemotherapy for gastric cancer.

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Introduction

Gastric cancer (GC) remains one of the leading causes of cancer-related mortality worldwide despite global advances in early detection and treatment strategies. According to GLOBOCAN 2022, GC ranks fifth in terms of incidence and cancer-related deaths,[1] with the highest burden reported in East Asia, Eastern Europe, and parts of South America. The prognosis of patients with GC is largely determined by the stage of the diagnosis. Unfortunately, a substantial proportion of patients present with locally advanced disease beyond the scope of immediate curative resection.

Surgical resection with adequate lymphadenectomy remains the cornerstone of curative-intent therapy for gastric adenocarcinomas. However, surgery alone yields suboptimal long-term outcomes due to the high risk of micrometastatic spread and disease recurrence. Consequently, multimodal treatment strategies have evolved to improve survival outcomes. The integration of perioperative or neoadjuvant chemotherapy into the treatment paradigm has shown significant benefits in terms of tumor downstaging, increased R0 resection rates, and improved overall survival.

The concept of perioperative chemotherapy was first validated in the pivotal MAGIC trial,[2] which demonstrated a survival advantage with the use of epirubicin, cisplatin, and 5-fluorouracil (ECF) compared to surgery alone. Subsequently, other regimens such as DCF (docetaxel, cisplatin, 5-FU) and FOLFOX (oxaliplatin, 5-FU, leucovorin) were explored, but their benefits were limited by their toxicity profiles or modest efficacy.

The FLOT (5-fluorouracil, leucovorin, oxaliplatin, and docetaxel) regimen has emerged as a superior alternative. The FLOT4-AIO trial[3] demonstrated that perioperative FLOT significantly improved overall survival (OS) (median OS 50 months vs 35 months) and pathological complete response (pCR) rates compared with ECF/ECX, with acceptable tolerability. These findings established FLOT as the standard of care for patients with resectable, locally advanced gastric or gastroesophageal junction adenocarcinoma.

Despite these encouraging results from randomized controlled trials, real-world data on the feasibility and outcomes of FLOT in diverse patient populations, particularly in low- and middle-income settings, remain limited. Differences in patient demographics, comorbidities, nutritional status, and access to supportive care can significantly influence treatment tolerance and survival outcomes. Therefore, evaluating the applicability of the FLOT regimen outside controlled trial environments is essential for understanding its true clinical impact.

This study aimed to assess the feasibility, safety, and clinical outcomes of perioperative FLOT chemotherapy in a real-world cohort of patients with resectable gastric adenocarcinoma treated at a tertiary care center.

Materials and Methods

Study Design and Population

This single-center retrospective observational study was conducted between April 2019 and April 2025 at a tertiary center. Data were collected from patients with resectable gastric adenocarcinoma who received perioperative FLOT chemotherapy as part of standard clinical practice.

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Eligible patients were aged 18–80 years with histologically confirmed gastric adenocarcinoma of clinical stage cT2 or higher and/or nodal involvement, according to the 8th edition of the American Joint Committee on Cancer (AJCC) Tumor–Node–Metastasis (TNM) classification. Clinical staging was performed using contrast-enhanced computed tomography (CT), upper gastrointestinal endoscopy with biopsy, and/or 18F-FDG positron emission tomography (PET) scans.

Patients with clinical stage T1 disease, distant metastases, or nonadenocarcinoma histology were excluded from the study.

Chemotherapy Regimen

All patients received perioperative FLOT chemotherapy, consisting of the following:

- 5-fluorouracil (2600 mg/m^2).
- Leucovorin (200 mg/m^2).
- Oxaliplatin (85 mg/m^2).
- Docetaxel (50 mg/m^2).

These were administered intravenously on day 1 of each 14-day cycle. Treatment delays or dose modifications were permitted at the discretion of the treating oncologist, based on toxicity, patient tolerance, or drug availability.

Outcome Measures

Primary Outcomes

The feasibility of perioperative FLOT chemotherapy was defined as the completion of at least four cycles.

Pathological complete response was defined as the absence of viable tumor cells on histopathological examination after neoadjuvant chemotherapy.

Secondary Outcomes

Surgical outcomes, treatment adherence, and adverse events (AEs) were also analyzed. Adverse events were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Radiological response was assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

Statistical Analysis

Demographic, clinical, and treatment-related variables were summarized using descriptive statistics. Categorical variables were expressed as frequencies and percentages, and continuous variables were expressed as medians with ranges. Statistical analysis was performed using the Jamovi software.

Results

Patient characteristics: Between April 2019 and April 2025, 44 patients received the neoadjuvant FLOT regimen. The patient characteristics are summarized in Table 1.

Twenty-seven patients (73%) were male, and 17 (27%) were female. The median age of the patients was 56 years (range, 26–71 years). The percentage of patients ≥56 years was 51%. Patients having comorbidities were 17 (37.7%), had comorbidities with a predominance of hypertension (20%) and diabetes (6%). 9 patients had hypertension (20%), 3 patients had type 2 diabetes (6%), and 3 patients had hypothyroidism (6%). One patient reported CAD with post-CABG status. One patient had CKD and was on medical management.

The most common clinical presentation was abdominal pain (48%) and weight loss (38%). Six patients reported recurrent vomiting (13%), four patients (8%) presented with gastric outlet obstruction, three patients had a history of melena (6%), two patients had dysphagia (4%), and one patient presented with incidental iron deficiency anemia (2%) (Table 2).

According to the Lauren classification, the histological type on diagnostic biopsy was diffuse-type adenocarcinoma noted in two patients (4%). The predominant histological grade was moderately differentiated adenocarcinoma, seen in 16 (51%) patients, with well differentiated histology in 3 (7%), poorly differentiated histology in 18 (29%), and 8 patients (18.2%) had signet ring cell histology. At the time of initial diagnosis, clinical stage T3–4 was reported in 87% (n = 29) of patients and nodal involvement in 80% (n = 41).

All patients were in good clinical condition, with an ECOG performance status (PS) of 0 or 1.

In the preoperative phase, 32 of 44 patients (64.4%) received at least four cycles of FLOT chemotherapy, regardless of dose reduction. Dose reduction or deintensification was performed in one patient (2%). Treatment delays occurred in two patients due to drug unavailability during the COVID period. The remaining 12 patients did not complete the entire treatment regimen.

Among the 32 patients who completed at least four FLOT cycles, 10 (24.4%) underwent surgical resection. Eight patients (22.2%) underwent total gastrectomy with D2 lymph node dissection (LND), while two patients underwent partial gastrectomy without LND. None of the patients achieved a pCR.

Among the 22 patients who did not undergo surgical intervention, nine experienced disease progression, six succumbed (4 due to nononcological causes and 2 as a result of febrile neutropenia with septic shock), and seven (11.1%) were lost to follow-up during the preoperative phase (2 due to symptom improvement, 1 due to apprehension regarding surgery, and 2 due to the prohibitive travel distances).

Table 1: Baseline characteristics

Characteristics	
Median age	56 years (26–71)
Gender	Male: 73%, Female: 27%
Comorbidities	37.7%
Hypertension (HTN)	20%
Diabetes	6%

Table 2: Symptoms at presentation

Symptoms	*Frequency (%)*
Abdominal pain	48
Weight loss	38
Recurrent vomiting	13
Gastric outlet obstruction	8

Among the cohort of 44 patients, 12 did not complete the four planned cycles of neoadjuvant FLOT therapy. Specifically, three patients underwent only one cycle, two patients completed two cycles, and seven patients received three cycles before becoming lost to follow-up. The reasons for this loss to follow-up were varied: symptom improvement (three patients), apprehension regarding surgery (two patients), fear of chemotherapy (three patients), preference for alternative or traditional medicine (one patient), and unspecified reasons for the remaining patients. Despite numerous attempts to contact these individuals through various communication channels, they remained unreachable (Fig. 1).

A total of 10 patients underwent adjuvant FLOT chemotherapy. Of these, six patients completed all four cycles, while two patients received two cycles, and two patients received one cycle. Among those who received fewer than four cycles of chemotherapy, one patient was lost to follow-up, and three patients experienced disease progression and subsequently received second-line CAPIRI chemotherapy.

Grade 3–4 adverse events (AEs) were observed in eight patients (18.1%). Cytopenias were the most frequently reported grade 3–4 AEs, with an incidence of 13.6%. Febrile neutropenia occurred in five patients, among whom two succumbed to progression to septic shock. Additionally, three patients required packed red blood cell (PRBC) transfusions following two cycles of chemotherapy. Intractable hiccups were documented in one patient, particularly during the initial two cycles of neoadjuvant FLOT chemotherapy.

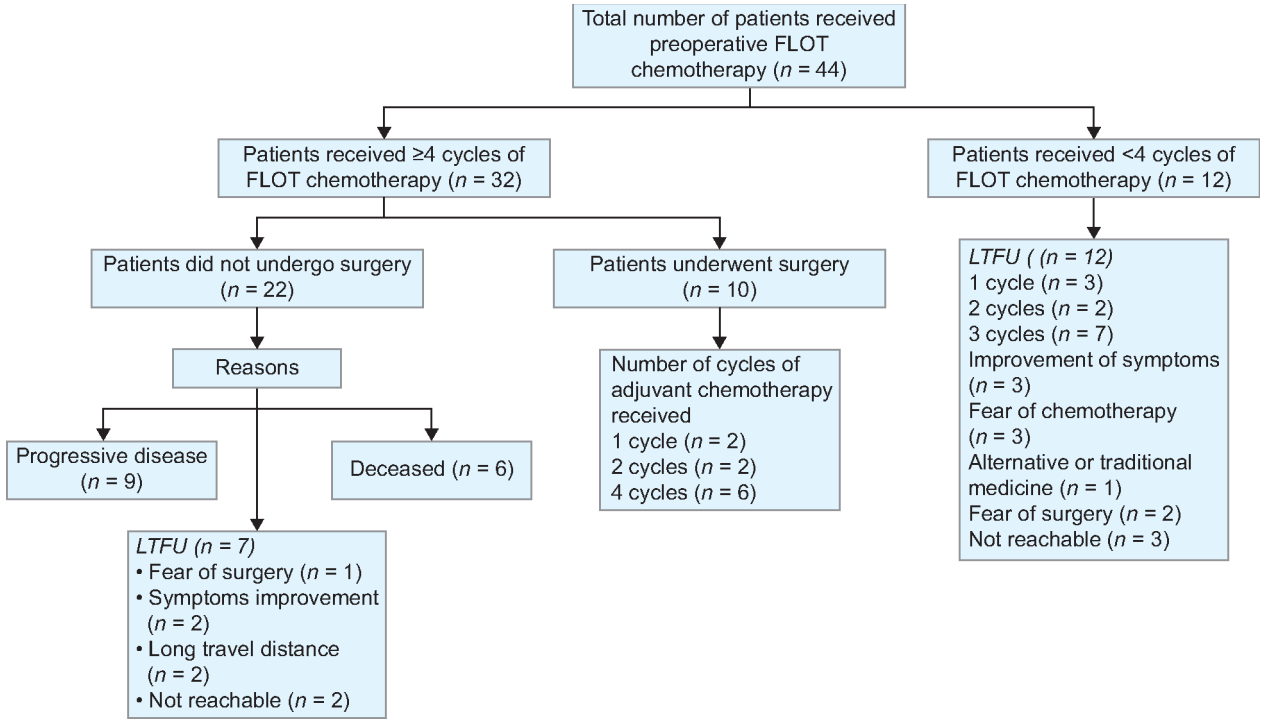

Fig. 1: Flow diagram of patient selection and treatment outcomes in patients receiving perioperative FLOT chemotherapy

Of the 44 patients, 20 (45.4%) were lost to follow-up. The primary reasons for this attrition were psychosocial factors, including fear of chemotherapy (n = 3) and fear of surgery (n = 2); socioeconomic factors, such as long travel distances (n = 2); and disease-related factors, such as improvement in symptoms (n = 1). Additionally, 20 patients could not be reached.

Discussion

This study aimed to assess the efficacy and safety of the neoadjuvant FLOT chemotherapy regimen in patients with locally advanced gastric cancer (GC), focusing on clinical outcomes, patient characteristics, surgical resection rates, and adverse events (AEs). Our findings are discussed in the context of published data on FLOT, particularly regarding patient demographics, chemotherapy adherence, surgical outcomes, and toxicity profiles.

The cohort consisted of 44 patients with a median age of 56 years, reflecting the typical age range of patients presenting with gastric cancer. A slight male predominance was observed, with 73% of patients being male, which is consistent with the established sex disparity in gastric cancer incidence. This sex distribution is commonly observed in Western and Asian populations, where men are more likely to be diagnosed with GC, particularly in advanced stages.[24]

In terms of comorbidities, 37.7% of the patients had at least one comorbidity, with hypertension (HTN) being the most common comorbidity (20%). These findings are consistent with other reports that suggest that cardiovascular disease is prevalent in patients with advanced gastric cancer.[5,6] The presence of comorbidities could complicate treatment strategies, especially in elderly patients, and may contribute to treatment delays or dose reductions, as was observed in 2% of our cohort.

The symptom profile in this cohort was also consistent with that typically seen in gastric cancer, with abdominal pain (48%) and weight loss (38%) being the most common presenting complaints. This is in line with the clinical presentation noted in other studies, where weight loss and abdominal discomfort were reported in the majority of patients with locally advanced GC.[7]

Histologically, moderately differentiated adenocarcinoma was the most common subtype (51%), followed by poorly differentiated adenocarcinoma (29%). This distribution aligns with the findings of large cohort studies, in which the majority of gastric cancers are classified as moderately or poorly differentiated.[8] Additionally, signet ring cell carcinoma, which is known for its poor prognosis, was observed in 18.2% of our patients, which is consistent with the expected incidence in gastric cancer cohorts.

At the time of diagnosis, the majority of patients (87%) were classified as having clinical stage T3–4 disease, and 80% had nodal involvement, underscoring the advanced nature of the disease at presentation. These findings reflect the late-stage diagnosis of GC, which is common because of nonspecific early symptoms and a lack of effective screening strategies.

In our cohort, 64.4% of the patients (32/44) received at least four cycles of FLOT chemotherapy. This adherence rate is comparable to that of the FLOT4 trial, in which over 60% of the patients completed the full course of neoadjuvant therapy. However, we observed a relatively high rate of progression or loss to follow-up during the preoperative phase, with nine patients progressing, six patients dying, and seven patients lost to follow-up. These figures highlight the challenges in managing high-risk populations with advanced disease, especially when combined with the socioeconomic and psychosocial barriers noted in our cohort.

Surgical resection was performed in 24.4% of the patients (10/32), which is lower than the 40–50% resection rates typically reported in large multicenter studies on neoadjuvant chemotherapy.[3] This discrepancy may be attributable to the high proportion of patients with metastatic disease discovered intraoperatively (two patients) or disease progression (seven patients) during treatment, highlighting the aggressive nature of advanced gastric cancer. In terms of resection type, eight patients underwent total gastrectomy, and two underwent partial gastrectomy, which aligns with typical surgical strategies based on tumor location and extent

of disease. Notably, no patient achieved a pathological complete response (ypT0), suggesting that although neoadjuvant FLOT therapy may reduce tumor burden, it does not guarantee a complete pathological response.

The safety profile in our cohort was consistent with the FLOT literature. The most commonly reported grade 3–4 adverse event (AE) was cytopenia (13.6%), which is a well-known dose-limiting toxicity of FLOT chemotherapy.[3,9] The need for blood transfusion in three patients and the occurrence of intractable hiccups in one patient, particularly during the first two cycles, were notable. The latter finding of hiccups is a rare but well-documented side effect of the FLOT regimen, and its occurrence may be more pronounced in the initial cycles of chemotherapy.[10]

Overall, the data from our cohort are in line with the findings from major studies, such as the FLOT4 trial, which demonstrated the efficacy of neoadjuvant FLOT chemotherapy in improving resectability in patients with locally advanced gastric cancer. However, the relatively low surgical resection rate and high rate of progression in our study suggest that while neoadjuvant FLOT is effective in downstaging tumors, not all patients achieve a sufficient tumor response to warrant surgery. This underlines the importance of refining patient selection and considering additional treatment modalities, including targeted therapies or immunotherapies, to improve the pathological completion rates.

Loss to follow-up (LTFU) represents a major barrier to optimal cancer care delivery, particularly in prolonged multimodal regimens, such as perioperative FLOT chemotherapy for gastric cancer. In this study, 45.4% of patients were lost to follow-up during the preoperative phase, despite initiating neoadjuvant chemotherapy. This high attrition rate adversely affected treatment completion, surgical resection rates, and overall clinical outcome assessments.

The causes of LTFU in this cohort were multifactorial, encompassing psychosocial, socioeconomic, disease-related, and healthcare system-related factors. Psychosocial causes included fear of surgery and chemotherapy, reflecting a limited understanding of disease prognosis and treatment intent. Symptom improvement following the initial chemotherapy cycles also contributed to discontinuation, suggesting a perceived resolution of the disease once the immediate symptoms subsided. Socioeconomic barriers, such as long travel distances, were additional contributors, reflecting the realities of treatment adherence in low- and middle-income countries. These findings align with prior studies identifying financial toxicity, geographical constraints, and limited health literacy as major determinants of nonadherence among oncology patients.[11,12]

Earlier reports on gastrointestinal malignancies have documented variable LTFU rates and follow-up completeness, with higher attrition in resource-limited settings.[13,14] The LTFU rate observed in the present study exceeds these figures, underlining the systemic challenges in maintaining continuity of care during perioperative chemotherapy. The long treatment duration, frequent hospital visits, and need for nutritional and psychosocial optimization may cumulatively contribute to patient fatigue and disengagement from care.

Loss to follow-up not only introduces attrition bias in outcome assessment but also has direct clinical implications. Patients who discontinue therapy prematurely are deprived of potential curative surgical interventions, which may negatively influence overall survival and disease control. Moreover, incomplete data regarding disease progression and treatment-related outcomes limit the generalizability of real-world evidence on FLOT efficacy. Therefore, addressing LTFU is essential for improving patient outcomes and the validity of clinical research.

Strategies to mitigate LTFU include implementing structured follow-up systems, patient navigation programs, and teleoncology models to maintain communication with patients from remote areas. Enhancing patient education regarding the importance of completing multimodal therapy, providing financial and travel assistance, and strengthening community-level cancer care networks may improve patient adherence. Incorporating psychosocial counseling and multidisciplinary support from oncologists, nurses, social workers, and psychologists can further alleviate fear and misinformation contributing to treatment discontinuation.

In summary, the high rate of LTFU observed in this study underscores the critical challenge in real-world gastric cancer management. Multifaceted interventions addressing patient, social, and systemic barriers are necessary to improve adherence, optimize treatment outcomes, and enhance the overall success of perioperative chemotherapy programs.

This study had several limitations. As this was a retrospective, single-center analysis with a small sample size, the findings may not be generalizable to broader populations. The high rate of loss to follow-up may have introduced attrition bias and limited the accurate assessment of survival and resection outcomes of the study.

Conclusion

Neoadjuvant FLOT chemotherapy remains the standard treatment for locally advanced gastric cancer with a potential for tumor downstaging. However, the lower-than-expected surgical resection rate and absence of pathological complete responses in our cohort highlight the aggressive nature of the disease and the need for improved treatment strategies to optimize patient outcomes.

Loss to follow-up was a key determinant of suboptimal outcomes, reflecting multifaceted psychosocial, economic, and systemic barriers to care. Addressing this requires a comprehensive, patient-centered approach that includes structured follow-up programs, tele-oncology services, financial and travel support, and improved patient education regarding treatment intent and benefits of treatment. By implementing such measures, healthcare systems can enhance adherence, reduce attrition, and ultimately improve patient outcomes and the success of treatment programs.

We propose that upfront surgery followed by adjuvant therapy may not be an inadequate treatment option for patients in this setting, particularly those who are likely to be noncompliant. Further prospective studies are required to substantiate this hypothesis.

Source of Support

Nil.

Conflict of Interest

None.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2024;74(3):229–263.
2. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355(1):11–20.
3. Al-Batran SE, Homann N, Pauligk C, et al. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial. Lancet 2019;393(10184):1948–1957.
4. Hui Y, Tu C, Liu D, et al. Risk factors for gastric cancer: A comprehensive analysis of observational studies. Front Public Health 2023;10:892468.
5. Keywani K, Borgstein ABJ, Eshuis WJ, et al. Neoadjuvant chemotherapy in older patients with gastric cancer undergoing surgery: A population-based cohort study. Gastric Cancer 2023;26(5):763–774.
6. Morishima T, Matsumoto Y, Koeda N, et al. Impact of comorbidities on survival in gastric, colorectal, and lung cancer patients. J Epidemiol 2019;29(3):110–115.

7. Sitarz R, Skierucha M, Mielko J, et al. Gastric cancer: Epidemiology, prevention, classification, and treatment. Cancer Manag Res 2018;10:239–248.
8. Hu B, Hajj NE, Sittler S, et al. Gastric cancer: Classification, histology and application of molecular pathology. J Gastrointest Oncol 2012;3(3):251–261.
9. Tastekin D, Paksoy N, Dogan I, et al. Fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) regimen in the first-line treatment of metastatic gastric cancer: a single-center experience. J Cancer Res Ther 2023;19(2):253–258.
10. Chang FY, Lu CL. Hiccup: Mystery, nature and treatment. J Neurogastroenterol Motil 2012;18(2):123–130.
11. Sundriyal D, Kapoor M, Antil P, et al. Factors associated with default of treatment and follow-up among patients with cancer: A cross-sectional study from a lower-middle-income country. JCO Glob Oncol 2024;10:e2400411.
12. Nizet P, Touchefeu Y, Pecout S, et al. Exploring the factors influencing adherence to oral anticancer drugs in patients with digestive cancer: a qualitative study. Support Care Cancer 2022;30(3):2591–2604.
13. Shand J, Stovold E, Goulding L, et al. Cancer care treatment attrition in adults: Measurement approaches and inequities in patient dropout rates—a rapid review. BMC Cancer 2024;24(1):1345.
14. Swaminathan R, Rama R, Shanta V. Lack of active follow-up of cancer patients in Chennai, India: Implications for population-based survival estimates. Bull World Health Organ 2008;86(7):509–515.