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ORIGINAL RESEARCH REPORT

Comparing the Safety and Efficacy of Intraluminal Brachytherapy vs Isolated Percutaneous Transhepatic Biliary Drainage with internalization for Unresectable Malignant Biliary Obstruction: A Prospective Observational Study

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Abstract

Background and objectives: **Intraluminal therapies, including brachytherapy, can locally destroy obstructing tumors and increase the duration of catheter/stent patency in patients with unresectable malignant biliary obstruction (MBO). In this prospective observational study, the safety and efficacy of percutaneous transhepatic biliary drainage (PTBD) followed by HDR intraluminal brachytherapy (ILBT) in the palliative treatment of malignant biliary obstruction was evaluated.**

Patients and methods: **In total, 66 MBO patients (January 2021 to March 2022) who were unfit for alternate treatment modalities were enrolled in our study and underwent percutaneous transhepatic biliary drainage (PTBD) with internalization. Additionally, 11 patients underwent subsequent ILBT, which was administered over two sessions (800 cGy each session, one week apart) with iridium-192 prescribed at 1.5 cm from the central axis of the catheter via a percutaneous biliary catheter. The second session was followed up by endoluminal stenting in the same sitting. Patients with an Eastern Cooperative Oncology Group (ECOG) status <4 and a 50% decline in bilirubin/<5 mg/dL on day 10 after PTBD were selected for ILBT. The biliary stent/catheter patency period, survival duration, mean bilirubin level (mg/dL) decline, and incidence of complications were evaluated.**

Results: **Among the sixty-six patients included and classified into ILBT or PTBD-only groups, the median survival period for the ILBT group vs PTBD group was 172 (84.5−273.5) days vs 45 (30.75−83) days ($p \leq 0.0001$) with an overall survival (OS) at 6 months of 62.34% vs 3.64% ($p \leq 0.0001$). The stent/catheter patency period of the ILBT group in comparison to the PTBD group was 172 (83−273.5) days vs 30 (20−42.5) days ($p \leq 0.0001$). No major treatment-related complications were observed in any of the patients.**

Conclusions: **ILBT with stenting is a safe option for improving stent patency and survival duration with minimal complications with the condition that patients are carefully selected.**

Keywords: Intraluminal brachytherapy, Malignant biliary obstruction, Percutaneous transhepatic biliary drainage

1. Introduction

Malignant biliary obstruction (MBO) encompasses a variety of malignant conditions resulting in obstructive jaundice. Common causes include gallbladder adenocarcinoma, cholangiocarcinoma, pancreatic adenocarcinoma, ampullary/duodenal adenocarcinoma, lymphoma, and compressive metastatic lymph nodes. The incidence of these neoplasms is increasing and has a poor prognosis due to diagnosis often occurring at an advanced stage [1]. Only 15−20% of these neoplasms

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are resectable at the time of presentation due to their invasiveness, late symptom appearance, and onset in elderly people [2,3].

Current treatments for locally advanced and metastatic tumors include chemoradiotherapy for downstaging of the tumor and/or palliative measures, such as stenting, to relieve biliary obstructions. Obstructive jaundice in patients undergoing chemotherapy may warrant the discontinuation of therapy due to the added hepatotoxic effects of some of the drugs [4]. Treatment options for the palliative therapy of biliary obstruction include surgical bypass procedures, such as hepaticoenterostomy, or minimally invasive procedures, such as the endoscopic or percutaneous insertion of biliary endo-prosthesis. Distal malignant biliary obstructions are typically managed by endoscopic stent placement, whereas hilar obstructions are more accessible through a percutaneous approach [5,6]. Despite improving the quality of life of the patients and alleviating many of the debilitating symptoms, such as cholestasis and pruritus, these treatments do not significantly improve survival [5].

As the malignant tumor is not removed using these treatment methods, the percutaneous transhepatic biliary drainage (PTBD) catheter or stent is prone to re-obstruction, either due to tumor ingrowth and/or overgrowth, resulting in biliary dilatation and cholangitis. This may require a repeat percutaneous puncture of the biliary radicles and repeat stenting. To address this problem and to prolong stent or catheter patency, the local destruction of the tumor mass is necessary. To this end, photodynamic therapy, intraluminal brachytherapy, and radiofrequency ablation have been increasingly used in recent years, and have been found to improve the prognosis, quality of life, and stent/catheter patency in most MBO patients. However, further studies are needed to determine the superiority of one modality over the other [5,6].

The combination of intraluminal brachytherapy (ILBT) with internalized PTBD has shown promising results in increasing the median survival time, as well as reducing morbidity, in comparison to drainage procedures alone [7,8]. In a systematic review by Taggar et al. on high dose rate (HDR) ILBT in the management of malignant biliary tract obstruction, it was found that despite significant heterogeneity in treatment regimens, ILBT resulted in a longer duration of stent patency with lower complication rates and toxicity [9]. An added advantage is that ILBT can be performed easily through internalized PTBD, and treatment can be safely adapted for lesions in right and left hepatic lobes, as well as common bile ducts.

Herein, the prospect of introducing ILBT into the palliative management of MBO using internalized PTBD in our institution was explored and its safety and efficacy, effect on survival period, symptomatic relief, and stent/PTBD patency was evaluated.

2. Materials and Methods

We prospectively analysed the safety and efficacy of HDR-ILBT in the palliative treatment of MBO patients using internalized PTBD with an emphasis on stent/catheter patency and overall survival. MBO patients that had been referred to our institute were screened for inclusion in the study. Patients with malignant biliary obstruction and an ECOG (Eastern Cooperative Oncology Group) status <4 with histopathologic proof of malignancy and no previous history of surgical drainage procedures from January 2021 and March 2022 were considered. Each patient underwent a thorough evaluation by an experienced physician and radiologist. A baseline investigative workup was done for all patients. Ultrasound (USG), computed tomography (CT), and/or magnetic resonance imaging (MRI) scans of the abdomen were performed before the procedure to identify the level and cause of obstruction and to assess the tumor. Histologic proof of malignancy was obtained in all cases either by fine needle aspiration cytology (FNAC) or by biopsy, whichever was feasible. The performance status of the patient was assessed by the physician and PTBD was performed by an experienced gastrointestinal radiologist. The decision of ILBT vs PTBD-only with internalization was decided by a physician (MG and AC) and interventional radiologist (SS) based on the assessment of consenting patients with ECOG status <4, once they showed adequate levels of bilirubin decline after PTBD internalization, it was a combined decision of the physician and intervention radiologist in consenting and affording patients. Patients were prepared for ILBT once their serum bilirubin levels decreased to 5 mg/dL or less than 50% of their baseline value.

2.1. PTBD with internalization technique

PTBD was performed using combined ultrasound and fluoroscopic guidance under local anesthesia. An anesthetic agent was locally infiltrated either on the left or right side, depending on the site of insertion. All patients received antibiotics (ceftriaxone, 1 g) one day prior to the procedure. The vital signs, including the patient's blood pressure, pulse rate, and oxygenation status, were monitored throughout the procedure. The ductal approach in PTBD was either left-sided or right-sided, depending on whether the primary or secondary confluences were patent or not, as well as the ductal union variation, as seen on MRCP, to ensure that the maximum amount of bile drainage could be performed with a single catheter. Under aseptic conditions, a fine needle (18G/22G depending on the degree of dilatation) was inserted into a dilated intrahepatic duct under USG guidance. A guidewire was then inserted through the needle into the biliary system and access was secured with a 6 F (15-cm long) sheath. Run was taken with diluted contrast to look for the level of obstruction (Fig. 1). The internalization of the PTBD was attempted with multiple catheters and guidewires. An interval of 7–10 days was used to enable the serum bilirubin levels to decrease and to allow for improvement in the patient's general condition. The status of biochemical parameters and symptoms were documented. After the bilirubin level fell below 5 mg/dL or less than 50% of their baseline value, ILBT was administered, provided the patient consented. After two sessions of ILBT administration, stenting was performed in the second sitting. If ILBT was not administered, then depending on the patient's general condition and his/her willingness for the procedure, stenting was performed or the patient was only treatment with the ring biliary catheter.

2.2. ILBT treatment planning and technique

Patients were administered ILBT once their serum bilirubin levels decreased to 5 mg/dL or less than 50% of their baseline value. The procedure was performed under intravenous antibiotic cover, which was administered both before and after the procedure to prevent cholangitis. In the fluoroscopy suite, a vascular sheath (7 F, 40 cm) was exchanged for the ring biliary catheter and a run was taken to look for the length of the malignant stricture with bony landmarks (vertebral levels) delineating the endpoints of the stricture (Fig. 1). Through this 7 F sheath with its tip in the duodenum, the blind-ended brachytherapy catheter (6 F, 150 cm) was then passed under fluoroscopic guidance and its tip was placed 1.5–2 cm beyond the distal end of the stricture (Fig. 1). The patient was then transferred to the simulator room where a radiopaque wire with markings was passed into the brachytherapy catheter, and orthogonal planning radiographs were obtained. Computerized planning was performed and the target volume to be irradiated was demarcated on simulation films (Fig. 1) maintaining a margin of 1.5–2 cm on either side of the stricture to compensate for respiratory movements. A dose of 800 cGy was prescribed at 1.5 cm from the centre axis of the catheter. The target dose was delivered using an Ir-192 source, once the patient was shifted to the HDR room. After the completion of ILBT, the patient was transferred back to the fluoroscopy suite, where the brachytherapy catheter was carefully withdrawn and the ring biliary catheter was reinstituted. One week later, a second session of the same treatment was carried out. All the patients fulfilling the criteria for ILBT completed two sessions and received a total brachytherapy dose of 1600 cGy in two fractions (800 cGy per fraction) one week apart by HDR. After the second dose of brachytherapy, stenting or internal catheter drainage was performed for all patients of the ILBT group as long as they had opted for the same.

2.3. Monitoring and follow-up

After the completion of the treatment, all patients were followed-up at two weeks and then at three-month intervals. At each follow-up, the patients were evaluated for symptoms and a biochemical workup was done.

Institutional ethical committee clearance was obtained before the commencement of the study

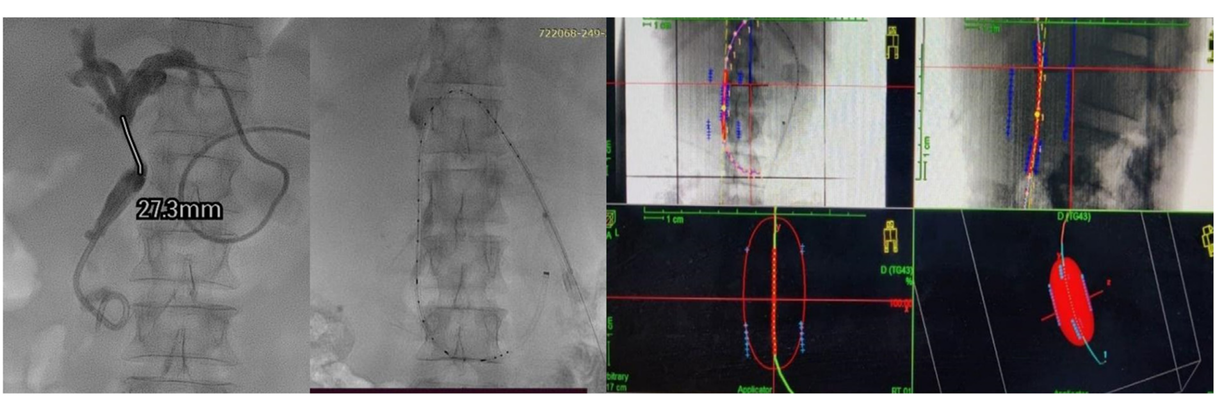

Fig. 1. Case showing stricturous narrowing of CHD. Localization was performed based on the vertebral level. The length was measured using calipers after calibration with catheter size, followed by dummy wire with markings and digital reconstruction for ILBT.

and written informed consent was taken from all patients prior to the procedures.

2.4. Statistical analysis

Microsoft Excel was used for data entry and Statistical Package for Social Sciences (SPSS) (ver 25.0) (IBM, Chicago, USA) was used for the final analysis. $P < 0.05$ was considered statistically significant. The normality of the data was verified using the Kolmogorov−Smirnov test. In the cases in which the data was not normal, non-parametric tests were used. Kaplan-Meier survival analysis curve was used to assess overall survival and stent/catheter patency in the ILBT + PTBD group and PTBD-only group, and the log-rank test was used for their comparison.

3. Results

A total of 81 patients with malignant biliary obstruction owing to various etiologies (Table 1) were included in this study. After the exclusion of 15 patients who had either uncorrectable coagulopathies, multiple strictures, or were non-consenting, the remaining sixty-six patients who satisfied the inclusion criteria were selected. Patients underwent PTBD with a successful internalization procedure conducted by a single experienced interventional radiologist. Among these, eleven consenting patients underwent ILBT following PTBD internalization once the required bilirubin levels were achieved. All of the patients in the ILBT group had subsequent stenting performed, while only five patients of the PTBD (internalized)-only group opted for stenting. At the time of analysis, six patients in the ILBT group were alive, while all the patients in PTBD (internalized)-only group had died. The corresponding consort chart, with patients considered under two separate groups, is displayed in Fig. 2.

The baseline characteristics of the patients in both groups are presented in Table 1. Gallbladder carcinoma was found to be the most common cause of malignant biliary obstruction in the study population (n = 30 [45.45%]) ($p = 0.742$). The majority of the patients had stricture at the level of the common hepatic duct (n = 28 [42.42%]) ($p = 0.824$). Additionally, a significant difference was observed between the ECOG statuses at the baseline between the two groups, with the majority of patients in the ILBT group having ECOG-2 statuses (n = 9 [81.82%]), while those in the PTBD-only group had ECOG-3 statuses (n = 49 [89.09%]) ($p < 0.0001$). The majority of the patients presented with symptoms of pain, jaundice, pruritus, loss of appetite, and weight loss. However, a significantly lower number of patients with weight loss (>10% in 6 months) were observed in the ILBT group (6 [54.55%]) at initial presentation in comparison to the PTBD group (50 [90.91%]) ($p = 0.002$).

The median (IQR) baseline serum bilirubin levels were 13.4 (9.35−19.25) mg/dL in the ILBT group and 15.5 (10.75−23.2) mg/dL in the PTBD-only group ($p < 0.0001$) (Table 1). The bilirubin levels after

Table 1. Comparison of baseline characteristics between the ILBT + PTBD and PTBD-only group

Baseline characteristics	ILBT + PTBD group (n = 11)	PTBD-only group (n = 55)	Total	*P*-value
Age (years)	52.36 (8.98)	59.56 (11.9)	58.36 (11.72)	0.062[a]
BMI (kg/m^2)	20.76 (2.69)	20.46 (3.38)	20.51 (3.26)	0.779[a]
Gender				
Female	7 (63.64%)	34 (61.82%)	41 (62.12%)	1[b]
Etiology				
Ca GB	4 (36.36%)	26 (47.27%)	30 (45.45%)	0.742[b]
Cholangiocarcinoma	3 (27.27%)	14 (25.45%)	17 (25.76%)	1[b]
Compressive Metastatic LN	3 (27.27%)	7 (12.73%)	10 (15.15%)	0.351[b]
Periampullary carcinoma	0 (0%)	2 (3.64%)	2 (3.03%)	1[b]
Ca head of pancreas	1 (9.09%)	6 (10.91%)	7 (10.61%)	1[b]
Level of stricture				
Right hepatic duct	1 (9.09%)	2 (3.64%)	3 (4.55%)	0.427[b]
Left hepatic duct	1 (9.09%)	6 (10.91%)	7 (10.61%)	1[b]
Confluence	1 (9.09%)	11 (20%)	12 (18.18%)	0.673[b]
Common hepatic duct	5 (45.45%)	23 (41.82%)	28 (42.42%)	0.824[b]
Common bile duct	3 (27.27%)	13 (23.64%)	16 (24.24%)	1[b]
ECOG				
2	9 (81.82%)	6 (10.91%)	15 (22.73%)	<0.0001[b]
3	2 (18.18%)	49 (89.09%)	51 (77.27%)	
Serum bilirubin (mg/dL) (at baseline)				
At baseline	13.4 (9.35−19.25)	15.5 (10.75−23.2)	15.45 (9.925−22.175)	0.286[c]

[a] Independent t-test.
[b] Fisher's exact test, mean (SD).
[c] Mann−Whitney test, median (interquartile range).

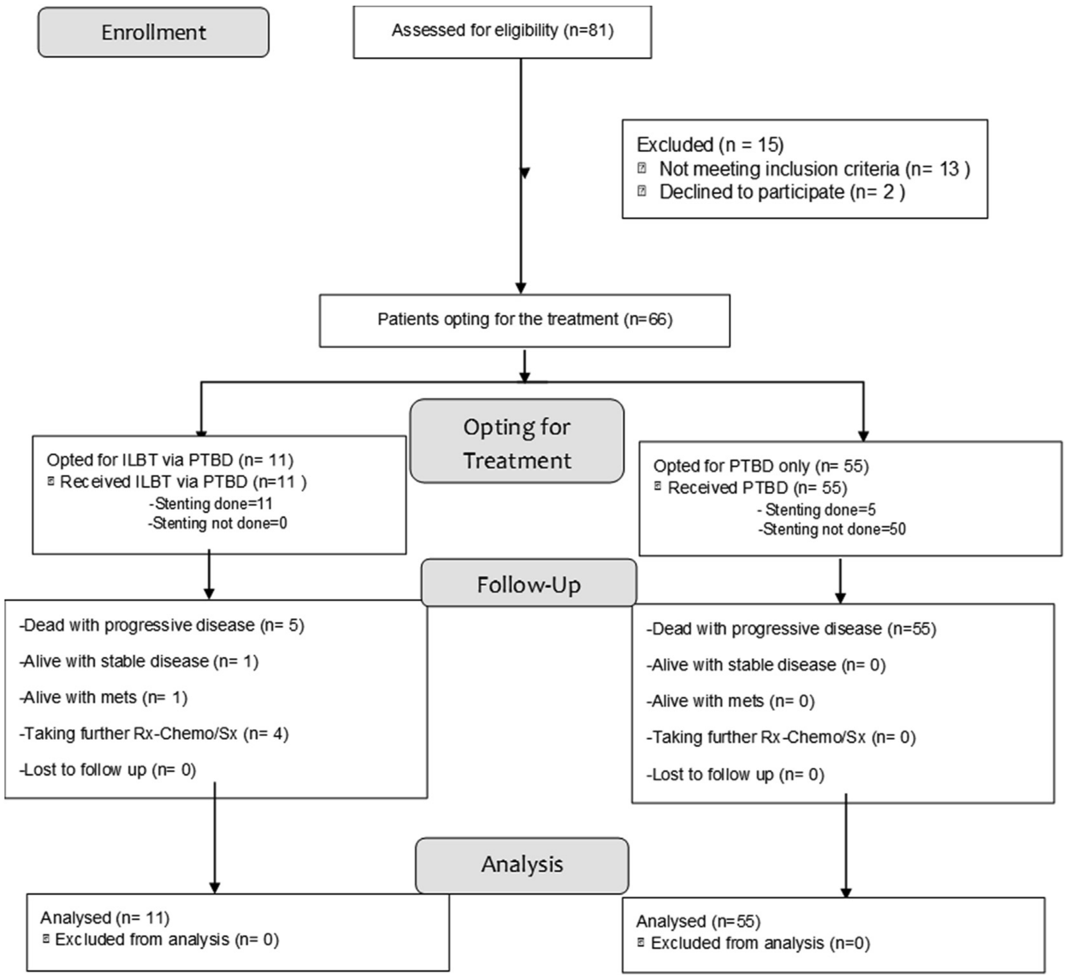

Fig. 2. Consort chart.

PTBD were significantly lower in the ILBT group (4.2 [3.6–7.1] mg/dL) in comparison to the PTBD-only group (8.3 [5.85–11.5] mg/dL) ($p = 0.004$). However, upon follow-up at 3, 6, and 9 months, this difference was not significant. A significant increase was also observed in the bilirubin levels in the PTBD group after 3 months, indicative of ongoing obstruction, as shown in Table 2.

Comparing the outcome parameters between the two groups, namely the median survival period (period from PTBD till endpoint: death/lost to follow-up/end of the study period) and the stent/catheter patency period (time for 50% bilirubin increase from nadir after PTBD/death), the ILBT group was found to have a significantly better and longer survival period. The median survival period for the ILBT group vs the PTBD group was 172 (84.5–273.5) days vs 45 (30.75–83) days ($p < 0.0001$) with an overall survival (OS) at 6 months of 62.34% vs 3.64% ($p < 0.0001$). The stent/catheter patency period of the ILBT group in comparison to the PTBD group was 172 (83–273.5) days vs 30 (20–42.5) days ($p < 0.0001$) (Table 3 and Fig. 3). Both parameters were analysed using Kaplan–Meier curves (Fig. 3) and compared with the log-rank test, which showed a statistically significant difference between the two

Table 2. Comparison of serum bilirubin (mg/dL) between the ILBT + PTBD and PTBD-only groups

Serum bilirubin (mg/dL)	At baseline	After PTBD	At 3 months	At 6 months	At 9 months
ILBT + PTBD group	13.4 (9.35–19.25)	4.2 (3.6–7.1)	3.2 (2.05–5.175)	2.4 (1.5–4.1)	0.76 (0.63–1.43)
PTBD-only group	15.5 (10.75–23.2)	8.3 (5.85–11.5)	6.7 (4.05–9.15)	16.75 (14.625–18.875)	–
Total	15.45 (9.925–22.175)	7.3 (5.125–10.875)	4.3 (2.3–7.25)	4.1 (1.95–13.4)	0.76 (0.63–1.43)
***P*-value**	0.286[a]	0.004[a]	0.093[a]	0.121[a]	–

[a] Mann–Whitney test, median (interquartile range).

Table 3. Comparison of parameters between the ILBT + PTBD and PTBD-only groups

Parameters	ILBT + PTBD group (n = 11)	PTBD-only group (n = 55)	Total	*P*-value
Survival period (days)	172 (84.5–273.5)	42 (24–60.5)	45 (30.75–83)	<0.0001[a]
Stent/catheter patency period (days)	172 (83–273.5)	30 (20–42.5)	32.5 (23–60)	<0.0001[a]

[a] Mann–Whitney test, median (interquartile range).

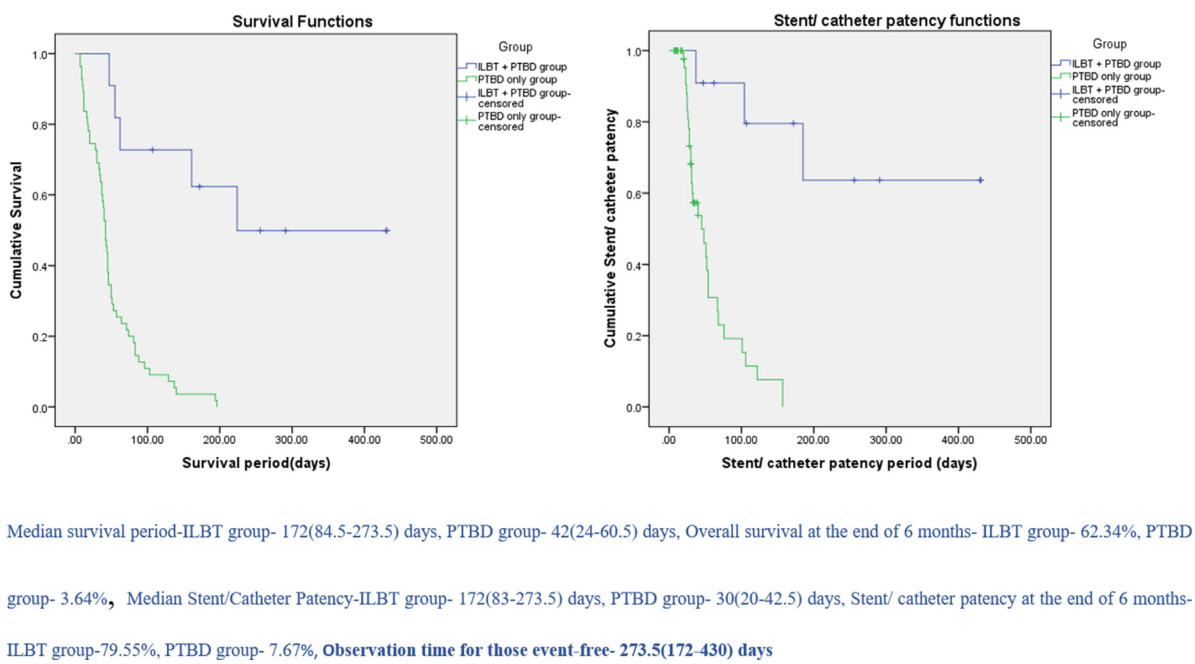

Fig. 3. Kaplan–Meier survival analysis curves of overall survival and catheter patency in the ILBT + PTBD and PTBD-only groups.

groups. As the study period was limited, the follow-up of the patients was defined as the estimate of the survivor function for the observation time for those patients that were event-free at the end of follow-up, which was calculated to be 273.5 (172–430) days.

3.1. Safety of ILBT group vs PTBD group

After PTBD with internalization, three patients (4.55%) developed mild probable cholangitis, all of whom recovered well with antibiotic treatment. Furthermore, five patients (7.58%) had pericatheteral leaks, which were managed with catheter upgradation, and one patient (1.52%) had catheter dislodgement, for which a new catheter was placed. Forty-two patients developed catheter blocks in later stages (63.64%), most likely due to tumor ingrowth or overgrowth (Table 4). Complications during and after ILBT treatment are presented in Table 4. All patients tolerated the treatment well. Many patients had mild pain, nausea, and vomiting, which was managed with analgesics and anti-emetics. None of the patients developed cholangitis/sepsis within 30 days after ILBT.

At the time of analysis, in the ILBT group, one patient was alive an stable, one was alive with liver metastasis, and four were alive and taking further treatment in the form of systemic chemotherapy (n = 6 [55.55%]). Five patients had died, two patients died of progressive malignancy, two patients died of

Table 4. Distribution of PTBD and ILBT complications in study population

PTBD complications	Frequency	Percentage
Pain	64	96.97%
Nausea and vomiting	8	12.12%
Bleeding	0	0.00%
Fever	4	6.06%
Cholangitis	3	4.55%
Pericatheral leak	5	7.58%
Catheter dislodgement	1	1.52%
Hemobilia	2	3.03%
Stent migration	0	0.00%
Catheter block	42	63.64%
Vascular injury	0	0.00%
Biliovenous fistula	0	0.00%
Pancreatitis	0	0.00%
Death	0	0.00%
ILBT complications		
Nausea and vomiting	3	27.27%
Local site pain	3	27.27%
Cholangitis	0	0.00%
Bleeding	0	0.00%
Duodenitis/ulcer	0	0.00%
Death	0	0.00%

sudden cardiac arrest, and one patient died of acute renal failure. No patients in the ILBT group were lost to follow-up.

In the PTBD (internalized)-only group, all patients had died. Seven patients were lost to follow-up. Of the remaining 55 patients, 38 patients died of progressive malignancy, four patients died of sudden cardiac arrest, and 13 patients died of acute renal failure.

4. Discussion

In patients with malignant biliary obstruction, PTBD internalization followed by ILBT was found to be a safe treatment option with minimal complications. This treatment may have positive impacts on overall survival and stent patency periods under the condition that patients are carefully selected. Limiting factors may include the etiology of obstruction, the local/metastatic spread of the disease, the patient's response to PTBD, and performance statuses. The PTBD catheter/stent, which decompresses the system, may be kept functional and patent for longer periods with ILBT.

In terms of the dosing regimen, we used HDR Ir-192 for ILBT, prescribing a dose of 1600 cGy in two fractions (800 cGy per fraction, one week apart), which was adapted from the pilot study by Aggarwal et al. [8] The results of this regimen confirmed the safety of the procedure at this dose, with minimal treatable complications. Common complications in ILBT patients include cholangitis, haemobilia, duodenal ulceration, bleeding, pancreatitis, and intrahepatic abscesses. Among the study population, some patients (4.55%) developed mild probable cholangitis after PTBD with internalization. However, this was restricted to the PTBD-only group, most likely owing to the poor performance statuses of these patients. Mild abdominal pain, nausea, and vomiting (27%) were observed after ILBT, which subsided after short-term treatment ith analgesics and antiemetics. We did not encounter any other serious complications. For palliative ILBT in patients with extrahepatic bile duct cancer, a dose of 30 Gy administered in six fractions at 1 cm from the radiation source was proposed by the HDR brachytherapy working group [10]. However, as discussed by Aggarwal et al. the optimum number and size of fractionation and total radiation dose in ILBT for extrahepatic biliary and pancreatic malignancies to achieve the best palliation with minimal complications remain up for debate. Relevant studies have reported various techniques, including HDR/LDR and/or the concurrent use of EBR, with variable doses in each series, hindering their comparison. In the present study, we opted for a lower dosing regimen to evaluate its efficacy on the basis of the pilot study conducted by Aggarwal et al. in an Indian population, which demonstrated good symptom control and a comparable overall survival with other brachytherapy dose schedules without the use of EBRT.

Regarding stent patency and survival, the ILBT group had a significantly better and longer survival period compared to the PTBD-only group. However, these results may not be fully reliable due to a lack of randomization, which may have led to the inclusion of several confounders. Furthermore, our stent/catheter patency periods and OS showed a poor prognosis in MBO patients, and were lower than those reported in systematic reviews by Xu et al. and Taggar et al. [9,11] This could be attributed to the shorter study period and case number in the present study. However, the median follow-up period for the ILBT group, which we defined as the event-free observation time, was 273.5 (172–430) days. This was a better predictor of the outcome in our study, which had 54.55% of patients in the ILBT group alive at the end of the study, owing to our shorter study period. The event-free observation time provides the most information regarding the stability of the Kaplan–Meier estimates in studies with shorter study periods[12]. This suggests that better outcomes can be obtained under conditions of stricter patient selection and earlier treatment initiation, as was observed in the present study.

The ILBT group and PTBD-only groups in our prospective study included 11 and 55 patients, respectively. This disparity in sample sizes may be inadequate for comparative studies. The ILBT group, which represents the case group, was not randomly allotted. Rather, the patients were given the choice to opt in, which may have led to the inclusion of significant confounding factors. The patients in our study had different etiologies resulting in MBO, which could represent one of the major confounders. Of the patients in the ILBT group, the majority had locally advanced disease and had a better response to PTBD internalization. The greater decline in bilirubin levels after PTBD internalization observed in this group may be due to the predominance of the intraluminal obstructive component, which was better relieved compared to the PTBD (internalization)-only group, in whom decreased levels were observed, albeit significantly lower. This may have led to a better response to ILBT in comparison to the other group, in which the majority of patients had extraluminal factors, including metastatic spread, outweighing the luminal obstruction. The baseline ECOG statuses of the ILBT group were significantly better than in the other group, which may represent a significant confounding factor in subsequent survival. The poorer overall survival and catheter/stent patency rates in the PTBD-only group may be attributed to these confounding factors, failure of matching, and the shorter study period. The survival times of the patients may be unreliable as the patients received further treatments based on their response to PTBD and ILBT, which hinders their analysis and comparison, as these directly affect the primary cause.

5. Conclusion

In the present study, despite the fact that the comparative analysis of the ILBT and PTBD-only groups may be unreliable due to numerous confounding factors, resulting from a lack of randomization, PTBD internalization followed by ILBT was found to be a safe treatment option in patients with malignant biliary obstruction with minimal complications. This treatment modality may have a positive impact on the overall survival and stent patency periods under the condition that the patients are carefully selected. Limiting factors include the etiology of obstruction, local/metastatic spread of the disease, patient response to PTBD, and patient performance statuses. Further randomised control studies are needed to better quantify the impact of ILBT in comparison to PTBD with internalization alone. Future studies should also seek to provide a consensus agreement regarding ILBT dosages and the addition of subsequent chemoradiotherapy, which could help in subsequent treatment standardization.

Conflict of interest

There are no conflicts of interest for any of the authors.

References

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA A Cancer J Clin 2020;70(1):7–30. https://doi.org/10.3322/caac.21590.

[2] Ryan DP, Hong TS, Bardeesy N. Pancreatic Adenocarcinoma. N Engl J Med 2014;371(11):1039–49. https://doi.org/10.1056/NEJMra1404198.

[3] Burke EC, Jarnagin WR, Hochwald SN, Pisters PWT, Fong Y, Blumgart LH. Hilar Cholangiocarcinoma: Patterns of Spread, the Importance of Hepatic Resection for Curative Operation, and a Presurgical Clinical Staging System. Ann Surg 1998;228(3):385–94. https://doi.org/10.1097/00000658-199809000-00011.

[4] Ray CE, Lorenz JM, Burke CT, et al. ACR Appropriateness Criteria Radiologic Management of Benign and Malignant Biliary Obstruction. J Am Coll Radiol 2013;10(8):567–74. https://doi.org/10.1016/j.jacr.2013.03.017.

[5] Boulay BR, Birg A. Malignant biliary obstruction: From palliation to treatment. WJGO 2016;8(6):498. https://doi.org/10.4251/wjgo.v8.i6.498.

[6] Deipolyi A, Covey A. Palliative Percutaneous Biliary Interventions in Malignant High Bile Duct Obstruction. Semin Intervent Radiol 2017;34(4):361–8. https://doi.org/10.1055/s-0037-1608827.

[7] Madhusudhan KS, Gamanagatti S, Srivastava DN, Gupta AK. Radiological interventions in malignant biliary obstruction. WJR 2016;8(5):518. https://doi.org/10.4329/wjr.v8.i5.518.

[8] Aggarwal R, Patel FD, Kapoor R, Kang M, Kumar P, Chander Sharma S. Evaluation of high-dose-rate intraluminal brachytherapy by percutaneous transhepatic biliary drainage in the palliative management of malignant biliary obstruction—A pilot study. Brachytherapy 2013;12(2):162–70. https://doi.org/10.1016/j.brachy.2012.06.002.

[9] Taggar AS, Mann P, Folkert MR, Aliakbari S, Myrehaug SD, Dawson LA. A systematic review of intraluminal high dose rate brachytherapy in the management of malignant biliary tract obstruction and cholangiocarcinoma. Radiother Oncol 2021;165:60–74. https://doi.org/10.1016/j.radonc.2021.10.011.

[10] Sahijdak WM. Principles and Practice of Brachytherapy Subir Nag, ed. Armonk, NY. Futura Publishing Co., 1997. 732 pp. $160. ISBN 0-87993-6540. *JNCI (J Natl Cancer Inst)*. 1998;90(12):932-933. https://doi.org/10.1093/jnci/90.12.932a.

[11] Xu X, Li J, Wu J, Zhu R, Ji W. A Systematic Review and Meta-analysis of Intraluminal Brachytherapy Versus Stent Alone in the Treatment of Malignant Obstructive Jaundice. Cardiovasc Intervent Radiol 2018;41(2):206–17. https://doi.org/10.1007/s00270-017-1827-6.

[12] Betensky RA. Measures of follow-up in time-to-event studies: Why provide them and what should they be? Clin Trials 2015;12(4):403–8. https://doi.org/10.1177/1740774515586176.