



CrossMark

Palliative treatment with radiation-emitting metallic stents in unresectable Bismuth type III or IV hilar cholangiocarcinoma

Jian Lu, Jin-He Guo, Hai-Dong Zhu, Guang-Yu Zhu, Yong Wang, Qi Zhang, Li Chen, Chao Wang, Tian-Fan Pan, Gao-Jun Teng

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/esmoopen-2017-000242>).

To cite: Lu J, Guo J-H, Zhu H-D, *et al.* Palliative treatment with radiation-emitting metallic stents in unresectable Bismuth type III or IV hilar cholangiocarcinoma. *ESMO Open* 2017;**2**:e000242. doi:10.1136/esmoopen-2017-000242

JL and J-HG contributed equally.

Received 3 July 2017
Accepted 14 July 2017

Department of Radiology, Zhong-Da Hospital, Southeast University, Nanjing, China

Correspondence to
Dr Gao-Jun Teng; gjteng@vip.sina.com

ABSTRACT

Background The emerging data for stenting in combination with brachytherapy in unresectable hilar cholangiocarcinoma are encouraging. The aim of this study was to evaluate the efficacy and safety of radiation-emitting metallic stents (REMS) for unresectable Bismuth type III or IV hilar cholangiocarcinoma.

Patients and methods Consecutive patients who underwent percutaneous placement with REMS or uncovered self-expandable metallic stent (SEMS) for unresectable Bismuth type III or IV hilar cholangiocarcinoma between September 2011 and April 2016 were identified into this retrospective study. Data on patient demographics and overall survival, functional success, stent patency and complications were collected at the authors' hospital.

Results A total of 59 patients were included: 33 (55.9%) in the REMS group and 26 (44.1%) in the SEMS group. The median overall survival was 338 days in the REMS group and 141 days in the SEMS group ($p < 0.001$). The median stent patency time was 385 days for REMS and 142 days for SEMS ($p < 0.001$). The functional success rate (87.9% vs 84.6%, $p = 0.722$) and incidence of overall complications (27.3% vs 26.9%, $p = 0.999$) did not differ in the two groups.

Conclusions Placement with REMS is safe and effective in palliation for unresectable Bismuth type III or IV hilar cholangiocarcinoma, and seems to prolong survival as well as patency of stent in these patients.

INTRODUCTION

Cholangiocarcinoma is a primary cancer of the bile ducts with a lower incidence in the West but a relatively higher incidence in the East, especially in Thailand, China and Korea.¹ Hilar cholangiocarcinoma accounts for about 50% of cholangiocarcinoma cases.² Due to the silent tumour growth, curative resection is often not suitable when diagnosed at the advanced stage.

For unresectable cases, endoscopic or percutaneous stent placement is considered the preferred palliation modality to relieve jaundice, cholangitis, pruritus and pain.³⁻⁴ However, the survival outcome

Key questions

What is already known about this subject?

► For patients with unresectable hilar cholangiocarcinoma, placement of self-expandable metallic stent (SEMS) is a recommended palliative modality to relieve pruritus, cholangitis, pain and jaundice. However, restenosis is a main pitfall after stent placement and limit the efficacy. One of the main reasons of stent restenosis is tumour infiltration.

What does this study add?

► Our results showed that placement with radiation-emitting metallic stents (REMS) achieved a longer patency of stent compared with placement with conventional SEMS, and the survival of patients in the REMS group was also better than that of patients in the SEMS group. Meanwhile, brachytherapy emitted from the biliary stent did not add to the incidence of complications.

How might this impact on clinical practice?

► Data from this study can be applied to aid clinical decision-making in the palliative treatment of unresectable hilar cholangiocarcinoma.

remains unsatisfactory and the stent patency is limited by tumour growth and/or incrustation.⁵⁻⁶ To provide local/systemic control of hilar cholangiocarcinoma, several stent-combined therapies have been used, such as chemotherapy, photodynamic therapy (PDT) and radiofrequency ablation (RFA), with improved outcomes.⁷⁻⁹

Many studies have suggested that hilar cholangiocarcinoma is responsive to radiation, such as external beam radiotherapy (EBRT) or brachytherapy.¹⁰⁻¹¹ Theoretically, compared with EBRT, brachytherapy could concurrently deliver a higher therapeutic dose to the tumour selectively with relative sparing of uninvolved biliary duct and normal organs or tissues. The first clinical

investigation of brachytherapy with Iridium-192 for unresectable hilar cholangiocarcinoma was advocated by Fletcher *et al* in 1981,¹² and the survival benefit has been demonstrated in subsequent clinical studies.^{13 14}

Recently, several studies have shown that stent placement plus brachytherapy with Iodine-125 appears to improve survival when compared with that with stent placement alone.^{15 16} A modified radiation-emitting metallic stent (REMS) loaded with Iodine-125 particles was developed, and promising results were demonstrated in malignant distal biliary obstruction.¹⁷ Herein, we conducted a retrospective study to compare the efficacy and safety of placement with an REMS and a conventional uncovered self-expandable metallic stent (SEMS) in patients with unresectable Bismuth type III or IV hilar cholangiocarcinoma.

METHODS

Patients

An electronic medical record at the authors' hospital was queried for consecutive patients with hilar cholangiocarcinoma between September 2011 and April 2016. This study included patients with inoperable hilar cholangiocarcinoma who underwent unilateral stent placement with REMS (REMS group) or conventional uncovered SEMS (SEMS group). The inclusion criteria were (1) newly diagnosed hilar cholangiocarcinoma with Bismuth type III or IV; (2) presentation of obstructive jaundice; (3) unresectable disease; and (4) mass <3 cm in diameter. The exclusion criteria were (1) Bismuth type I or II; (2) history of biliary stent, endoscopic biliary drainage or percutaneous transhepatic biliary drainage (PTBD), surgery, chemotherapy and radiotherapy; (3) suffered from malignancy other than cholangiocarcinoma; and (4) incomplete data. The study was approved by the local ethics committees. Each patient gave written informed consent prior to treatment.

Technique

A total of 59 biliary stents were unilaterally inserted. The diameter of the placed stents was 10 mm in both groups. The REMS was structured as a double-layer composition: an inner uncovered SEMS and an outer Iodine-125 seed-loaded stent, which would be assembled after deployed into the target biliary tract.⁹ The prescription dose of Iodine-125 seeds (CIAE-6711; Chinese Atomic Energy Science Institution, Beijing, China) was planned and calculated according to the Treatment Planning System (FTT Technology, Beijing, China). Prior to stent placement, the Iodine-125 seeds were assembled to capsules, which were attached on the surface of outer stent. The median calculated surface radiation dose at the dose prescription point was 47.0 Gray (range, 29.9–61.3).

A standard PTBD procedure was performed under ultrasonic and fluoroscopic guidance. In the REMS group, following coaxial dilatation with balloon dilator catheter, the outer Iodine-125 seeds-loaded stent was first

introduced through a 10-French sheath and deployed across the diseased biliary duct over a stiff guidewire. Then, an inner uncovered SEMS (Nanjing Micro-Tech, Nanjing, China) was immediately introduced through the same guidewire to overlap the outer stent (online supplementary figure S1). In the SEMS group, an uncovered SEMS was inserted to the dominant lobe of the targeted biliary duct. Unilateral (type III) or bilateral (type IV) external drainage catheter (Cook Medical, Bloomington, Indiana, USA) was placed above the level of the stricture to remove any possible blood clots or sludge, which would be retrieved 1 week later if the drainage was evaluated successful. Radiation safety and management with regard to the REMS were conducted according to the criteria from the International Commission on Radiological Protection.

Outcomes and definitions

Overall survival was defined as the time from stent placement to death or last visit. Functional success was defined as a decrease in serum bilirubin to less than 50% of the pretreatment level within the first week. Patency of stent refers to the interval from stent placement to the recurrence of stent restenosis. Stent restenosis was defined as the redevelopment of symptomatic and biochemical evidence of biliary obstruction with radiological confirmation. Complications occurring within 30 days and after

Table 1 Baseline characteristics of the study population

Variables	REMS group (n=33)	SEMS group (n=26)	p Value
Sex			0.351
Male	18	11	
Female	15	15	
Age, year	66.2±10.0	64.0±9.7	0.397
BMI, kg/m ²	21.2±1.9	20.3±1.8	0.081
Serum bilirubin level, µmol/L	209.4±101.1	225.7±111.4	0.560
Duration of symptoms, days	36.5±24.5	41.8±19.5	0.372
Diagnostic method			0.642
Cytology	21	15	
Clinical diagnosis	12	11	
Bismuth classification			0.602
Type III	20	14	
Type IV	13	12	
Extent of disease			0.388
Locally advanced	22	20	
Metastatic	11	6	

BMI, body mass index; REMS, radiation-emitting metallic stent; SEMS, self-expandable metallic stent.

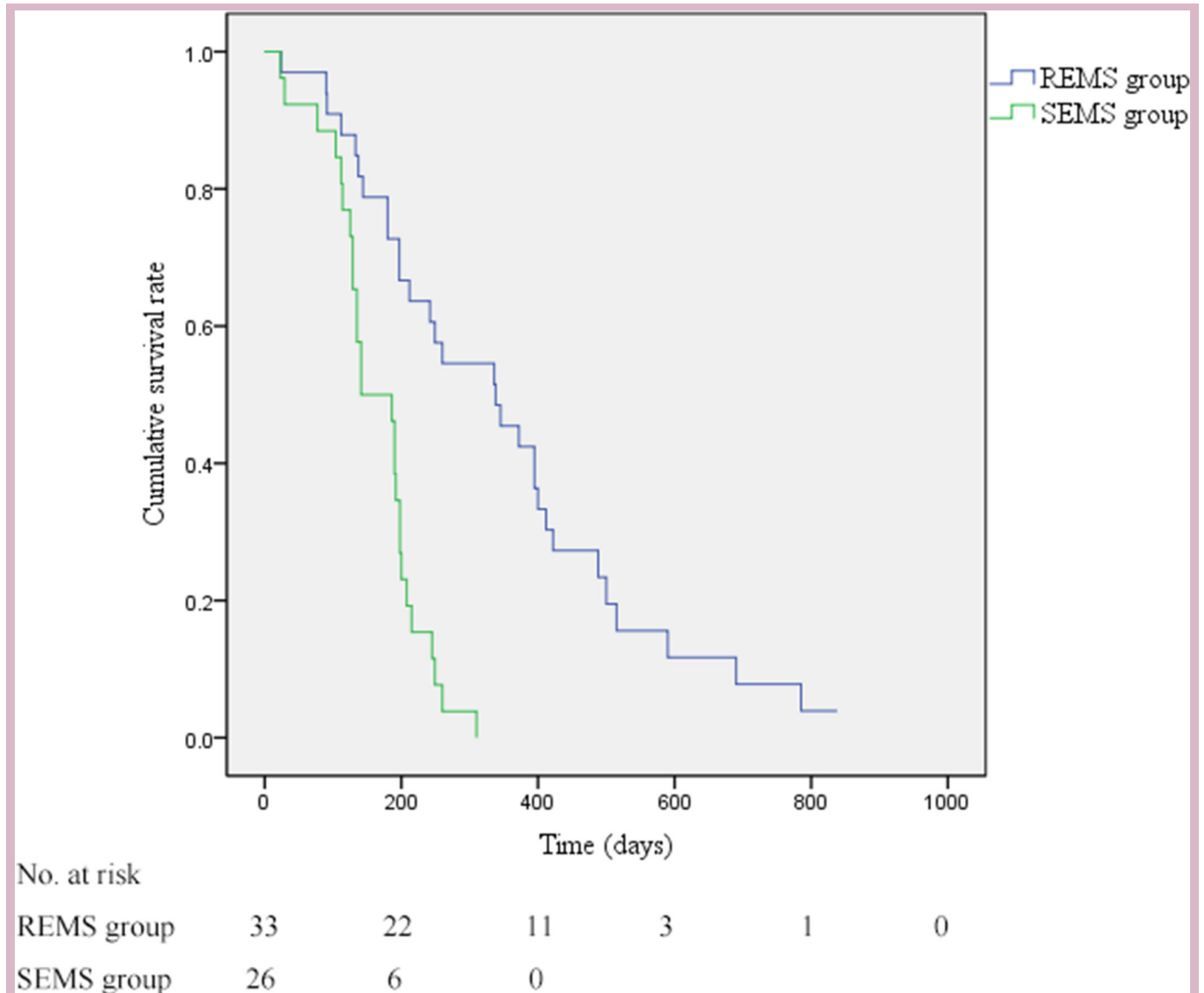


Figure 1 Comparison of survival between the REMS group and the SEMS group. REMS, radiation-emitting metallic stent; SEMS, self-expandable metallic stent.

30 days after stent placement were classified, respectively, as early and late complications.

Follow-up and data collection

Patients were required to undergo routine follow-up at 1 week, monthly for first 6 months and then every 3 months after treatment. The routine follow-up protocol included clinical signs, laboratory tests and imaging examinations (plain film, ultrasound, abdominal CT and magnetic resonance cholangiopancreatography). The clinical, laboratory and radiological records of the recruited patients in this study were reviewed and collected from the electronic medical record.

Statistical analysis

The numerical data with normal distribution were expressed as mean \pm SD, while data with non-normal distribution were expressed as median (IQR). Continuous variables were compared using the t-test or Mann-Whitney U

test for variables with a non-normal distribution. Categorical variables were compared using the X^2 test or Fisher's exact test. Overall survival time analyses were performed with the Kaplan-Meier method and log-rank test. Univariate Cox proportional hazards regression analyses were performed to estimate potential factors associated with survival. An HR with 95% CI was calculated for each variable. All variables with $p < 0.10$ in univariate analyses were included in the subsequent multivariate analysis. A p value less than 0.05 was considered statistically significant. All data analyses were performed using statistical software (SPSS V.19.0).

RESULTS

Clinical characteristics

A total of 59 patients with hilar cholangiocarcinoma were included: 33 patients (55.9%) in the REMS group and 26 (44.1%) in the SEMS group (online supplementary

Table 2 Univariate and multivariate analyses of prognostic factors for survival

Univariate analysis				Multivariate analysis		
Variable	HR	p Value	95% CI	HR	p Value	95% CI
Age, year						
<65	1					
≥65	1.409	0.208	0.826 to 2.403			
Sex						
Male	1					
Female	1.155	0.596	0.678 to 1.969			
BMI, kg/m ²						
<20	1					
≥20	0.950	0.861	0.532 to 1.694			
Total bilirubin level, μmol/L						
<200	1					
≥200	1.605	0.082	0.942 to 2.737			
Duration of symptoms, days						
<30	1					
≥30	1.315	0.328	0.760 to 2.275			
Bismuth type						
Type III	1					
Type IV	1.756	0.047	1.008 to 3.059			
Distant metastasis						
Absent	1			1		
Present	0.340	0.001	0.181 to 0.637	0.304	<0.001	0.159 to 0.584
Stent type						
REMS	1			1		
SEMS	4.295	<0.001	2.204 to 8.371	6.456	<0.001	2.355 to 9.225
Poststenting chemotherapy						
Yes	1					
No	2.007	0.090	0.896 to 4.492			

BMI, body mass index; REMS, radiation-emitting metallic stent; SEMS, self-expandable metallic stent.

figure S2). Overall, the two groups were comparable for the demographic and disease factors at baseline (table 1). After stent placement, eight patients (13.6%) underwent subsequent gemcitabine-based chemotherapy. No patients received additional EBRT, brachytherapy, PDT or RFA.

Efficacy

The median follow-up time was 267 days (IQR, 178–402 days). To date, three patients (5.1%) in the REMS group remained alive, and the other 56 patients (94.9%) had died, of whom 19 cases died of cancer cachexia, 17 of liver failure from disease burden, 7 of cholangitis, 5 of pulmonary failure, 3 of haemobilia, 1 of pulmonary embolism and 4 of unclear reasons. The median overall survival was 338 days (IQR, 180–488 days) in the REMS group and 141 days (IQR, 125–200 days) in the SEMS group, respectively ($p<0.001$) (figure 1). The cumulative survival rate at 90, 180 and 360 days was 93.9% vs 88.5%, 72.7% vs 50.0%,

and 45.5% vs 0 in the REMS group and SEMS group, respectively ($p<0.001$). On univariate analysis, Bismuth type, distant metastasis and stent type were significantly associated with survival in this study. On multivariate Cox analysis, distant metastasis and stent type were jointly demonstrated as independent prognostic factors for survival (table 2).

Functional success was noted in 87.9% of patients (29/33) in the REMS group and 84.6% of patients (22/26) in the SEMS group, respectively ($p=0.722$). The bilirubin level was reduced significantly from 209.4 ± 101.1 μmol/L to 62.8 ± 47.2 μmol/L in the REMS group ($p<0.001$), and from 225.7 ± 111.4 mg/dL to 66.7 ± 53.0 μmol/L in the SEMS group ($p<0.001$).

Stent occlusion occurred in 8 (24.2%) patients of the REMS group and 11 (43.2%) of the SEMS group, respectively ($p=0.169$). The median stent patency time was 385 days (IQR, 375–670 days) for REMS and 142 days (IQR,

Table 3 Early and late complications in the two groups

Variable	REMS group (n=33)	SEMS group (n=26)
Early complications, n (%)		
Abdominal pain	1 (3.0%)	1 (3.8%)
Bleeding	2 (6.1%)	0
Cholangitis	1 (3.0%)	1 (3.8%)
Late complications, n (%)		
Sepsis	0	1 (3.8%)
Cholangitis	2 (6.1%)	3 (11.5%)
Thrombocytopenia	2 (6.1%)	0

REMS, radiation-emitting metallic stent; SEMS, self-expandable metallic stent.

125–198 days) for SEMS, respectively ($p < 0.001$). Percutaneous reintervention was conducted in 10 patients: two patients with uncovered metal stent, seven patients with PTBD, while the other three patients refused sequential therapy due to the poor systemic condition.

Safety

There was no significant difference in the incidence of overall complications (27.3% vs 26.9%, $p = 0.999$) between the two groups (table 3). Early complications occurred in five patients (15.2%) in the REMS group and three (11.5%) in the SEMS group ($p = 0.976$), respectively. Two patients (one in each group) required analgesics for 48 hours after stent placement. One patient in the REMS group experienced bleeding after the procedure and was treated by coagulation treatment. Cholangitis developed in three patients (two in the REMS group and one in the SEMS group) and were treated by intravenous antibiotics. All the above complications were resolved as a result of these treatments. There was no procedure-related mortality. Late complications were seen in 12.1% (4/33) of patients in the SEMS group and 15.4% (4/26) of patients in the REMS group ($p = 0.722$). Sepsis was observed in one patient of the SEMS group. Two patients developed thrombocytopenia after REMS placement. The three patients above improved after conservative treatment. Additionally, a total of five patients experienced late cholangitis, of whom one patient was recovered after treatment with intravenous antibiotics and the remaining were treated by PTBD.

DISCUSSION

This study aimed to compare the efficacy and safety of placement with REMS and conventional SEMS for unresectable Bismuth type III or IV hilar cholangiocarcinoma. The findings suggest that REMS could provide a longer survival and patency than SEMS, without adding to the rate of complications.

For unresectable hilar cholangiocarcinoma, palliative drainage using an uncovered SEMS has been a preferred strategy to obtain symptomatic improvement, especially

for patients with an expected survival of more than 3 months.^{3 11} However, it is often challenging to achieve long-term patency and survival by stenting alone because of tumour growth. The combination of stent placement with brachytherapy has been reported with promising results in malignant biliary stricture.^{11 13 14} Due to the numerous advantages, including an effective radiation radius of 20 mm, a half-life of 60 days and rapid dose attenuation at distance, Iodine-125 has been the preferred choice of brachytherapy source.^{15 16}

There exists controversy as to whether unilateral or bilateral biliary stenting should be done when hilar strictures interrupt the main and the right/left secondary hepatic confluence.⁶ Generally, bilateral stenting was expected to achieve better biliary drainage, lower the risk of cholangitis and prolong stent patency. However the technique difficulty of bilateral stenting is challenging. In the present study, the use of unilateral placement of REMS aimed to deliver a close brachytherapy to target tumour, concurrently with the immediate recanalisation of the biliary tract. Due to its radiation-sensitive nature, the interdiction between the main and secondary hepatic biliary tract could be relieved. Subsequently, a comparably adequate drainage could be achieved by the unilateral REMS placement. Moreover, the long-term patency of unilateral placement with the present REMS was more than twice as long as that with the SEMS with significant difference, and also seems superior to the previous results of unilateral or bilateral placement with SEMS.^{5 6}

In comparison with patients in the SEMS group, those in the REMS group obtained an obvious survival advantage, especially in the long-term survival 1 year after treatment. Based on the balanced patient characteristics between the two groups, we may speculate that the added brachytherapy may help to improve survival of patients by delaying tumour growth. The survival obtained in the REMS group seems longer than that found using unilateral or bilateral SEMS,^{5 6} or intraluminal I-192 brachytherapy with or without EBRT.^{13 14} The survival advantage of REMS over the bilateral SEMS may be obtained from the longer patency of REMS, which could provide a sustained biliary drainage after long-term brachytherapy.

In the management of type III or IV hilar obstruction, endoscopic stent placement is often challenging and more complex than in distal malignant biliary obstruction.^{4 18} In the present study, the percutaneous approach was chosen for a higher technical success rate, lower complication rate and a comparable drainage success rate, compared with the endoscopic approach.^{19 20} Procedure-related bleeding due to the arteriovenous injury was a major concern during percutaneous stent placement.²¹ Theoretically, the use of a relative small delivery sheath may decrease the rate of bleeding. However, in the design of REMS, if the radioactive seeds were directly attached on the surface of stent, a large delivery system would be required. Therefore, the REMS was designed as a double-layer structure for minimal delivery sheath (10 French). The incidence (6.1%) of bleeding in the REMS

group was acceptable. Moreover, the rates of both early and late complications in the REMS group were similar to the results of the SEMS group and previous reports using REMS.^{22,23} These results suggest that the approach of percutaneous placement with such an REMS is technically safe.

There are some limitations to this study. First, the evaluation of tumour response was abandoned in the REMS group because of the measurement difficulty caused by metallic and radioactive artefact on images. Second, a portion of patients (39%) were diagnosed of hilar cholangiocarcinoma by clinical pretensions without the confirmation by biopsy. Third, this was a non-randomised, retrospective study without a well-designed protocol. Further prospective, randomised controlled trials are warranted.

In conclusion, placement with REMS is safe in palliation for unresectable Bismuth type III or IV hilar cholangiocarcinoma, and seems to prolong survival of patients as well as patency of stent.

Acknowledgements The authors thank Jie Min from Southeast University for her assistance in the statistical analyses.

Contributors GJT and JHG were involved in the study supervision, study conception and design. JL analysed and interpreted the data and drafted the manuscript. HDZ was involved in the critical revision of the manuscript. G-YZ, YW, LC and QZ were involved in the percutaneous stent placement. CW was involved in the data collection and regular follow-up. TFP was involved in the brachytherapy treatment planning. All the authors had full access to all of the data and gave final approval of the version to be published.

Competing interests None declared.

Patient consent Obtained.

Ethics approval IEC for Clinical Research of Zhong-Da Hospital, Affiliated to Southeast University.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement To get access to data in this study, please contact gjteng@vip.sina.com (email) and +86 25 83272121 (Tel).

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

© European Society for Medical Oncology (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

1. Bridgewater JA, Goodman KA, Kalyan A, *et al.* Biliary Tract Cancer: Epidemiology, Radiotherapy, and Molecular Profiling. *Am Soc Clin Oncol Educ Book* 2016;35:e194–e203.
2. Razumilava N, Gores GJ. Cholangiocarcinoma. *Lancet* 2014;383:2168–79.
3. Dumonceau JM, Tringali A, Blero D, *et al.* Biliary stenting: indications, choice of stents and results: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. *Endoscopy* 2012;44:277–98.
4. Rerknimitr R, Angsuwatcharakon P, Ratanachu-ek T, *et al.* Asia-Pacific consensus recommendations for endoscopic and interventional management of hilar cholangiocarcinoma. *J Gastroenterol Hepatol* 2013;28:593–607.
5. Rerknimitr R, Kongkam P, Kullavanijaya P. Outcome of self-expandable metallic stents in low-grade versus advanced hilar obstruction. *J Gastroenterol Hepatol* 2008;23:1695–701.
6. Jang SI, Lee DK. Update on Pancreatobiliary Stents: Stent Placement in Advanced Hilar Tumors. *Clin Endosc* 2015;48:201–8.
7. Valle JW, Wasan H, Johnson P, *et al.* Gemcitabine alone or in combination with cisplatin in patients with advanced or metastatic cholangiocarcinomas or other biliary tract tumours: a multicentre randomised phase II study - The UK ABC-01 Study. *Br J Cancer* 2009;101:621–7.
8. Moole H, Tathireddy H, Dharmapuri S, *et al.* Success of photodynamic therapy in palliating patients with nonresectable cholangiocarcinoma: A systematic review and meta-analysis. *World J Gastroenterol* 2017;23:1278–88.
9. Patel J, Rizk N, Kahaleh M. Role of photodynamic therapy and intraductal radiofrequency ablation in cholangiocarcinoma. *Best Pract Res Clin Gastroenterol* 2015;29:309–18.
10. Bowling TE, Galbraith SM, Hatfield AR, *et al.* A retrospective comparison of endoscopic stenting alone with stenting and radiotherapy in non-resectable cholangiocarcinoma. *Gut* 1996;39:852–5.
11. Larghi A, Tringali A, Lecca PG, *et al.* Management of hilar biliary strictures. *Am J Gastroenterol* 2008;103:458–73.
12. Fletcher MS, Brinkley D, Dawson JL, *et al.* Treatment of high bile duct carcinoma by internal radiotherapy with iridium-192 wire. *Lancet* 1981;2:172–4.
13. Mattiucci GC, Autorino R, Tringali A, *et al.* A Phase I study of high-dose-rate intraluminal brachytherapy as palliative treatment in extrahepatic biliary tract cancer. *Brachytherapy* 2015;14:401–4.
14. Mukewar S, Gupta A, Baron TH, *et al.* Endoscopically inserted nasobiliary catheters for high dose-rate brachytherapy as part of neoadjuvant therapy for perihilar cholangiocarcinoma. *Endoscopy* 2015;47:878–83.
15. Hasimu A, Gu JP, Ji WZ, *et al.* Comparative Study of Percutaneous Transhepatic Biliary Stent Placement with or without Iodine-125 Seeds for Treating Patients with Malignant Biliary Obstruction. *J Vasc Interv Radiol* 2017;28:583–93.
16. Yang M, Yan Z, Luo J, *et al.* A pilot study of intraluminal brachytherapy using (125I) seed strand for locally advanced pancreatic ductal adenocarcinoma with obstructive jaundice. *Brachytherapy* 2016;15:859–64.
17. Zhu HD, Guo JH, Zhu GY, *et al.* A novel biliary stent loaded with (125I) seeds in patients with malignant biliary obstruction: preliminary results versus a conventional biliary stent. *J Hepatol* 2012;56:1104–11.
18. Cotton PB, Eisen G, Romagnuolo J, *et al.* Grading the complexity of endoscopic procedures: results of an ASGE working party. *Gastrointest Endosc* 2011;73:868–74.
19. Paik WH, Park YS, Hwang JH, *et al.* Palliative treatment with self-expandable metallic stents in patients with advanced type III or IV hilar cholangiocarcinoma: a percutaneous versus endoscopic approach. *Gastrointest Endosc* 2009;69:55–62.
20. Moole H, Dharmapuri S, Duvvuri A, *et al.* Endoscopic versus Percutaneous Biliary Drainage in Palliation of Advanced Malignant Hilar Obstruction: A Meta-Analysis and Systematic Review. *Can J Gastroenterol Hepatol* 2016;2016:1–8.
21. Hamada T, Yasunaga H, Nakai Y, *et al.* Severe bleeding after percutaneous transhepatic drainage of the biliary system: effect of antithrombotic agents—analysis of 34 606 cases from a Japanese nationwide administrative database. *Radiology* 2015;274:605–13.
22. Kim JY, Kang DH, Kim HW, *et al.* Usefulness of slimmer and open-cell-design stents for endoscopic bilateral stenting and endoscopic revision in patients with hilar cholangiocarcinoma (with video). *Gastrointest Endosc* 2009;70:1109–15.
23. De Palma GD, Pezzullo A, Rega M, *et al.* Unilateral placement of metallic stents for malignant hilar obstruction: a prospective study. *Gastrointest Endosc* 2003;58:50–3.