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Appendix 1
For each case or control, the following variables were extracted:
1) demographical variables; 2) primary disease and indication (i.e. malignant vs. benign; level of the stenosis; eventual previous failed ERCP; eventual disconnected left/right hepatic ducts); 3) technical aspects (ie, stent type, length and diameter; procedure duration); 4) biochemical variables (total bilirubin before procedure, at day 7 and at nadir (with time-to-nadir); absolute and relative reduction); 5) adverse events; 6) outcomes (i.a. post-procedure hospital stay; time-to-chemotherapy initiation/resumption, dysfunction, eventual time-to-dysfunction and rescue procedures; post-procedural reinterventions; deaths and causes of death).
For EUS-IBD additional variables were evaluated: ascites or liver metastasis at the moment of the procedure; calibre and type of needle used to puncture the biliary tree; pre- and post-procedural C-reactive protein (CRP).

Appendix 2
See **Fig. 2.** We categorized the procedures following EUS-guided intrahepatic access as: 1) EUS-guided rendez-vous (e-RV) when EUS-IBD was used to allow antegrade trans-papillary placement of a guidewire, which was subsequently used for final retrograde cannulation; 2) EUS-guided antegrade stenting (e-AS) when a guidewire was advanced through the stenosis and subsequently a conventional self-expandable metal stent (SEMS) was advanced trans-gastric and trans-hepatic over the guidewire to cross the stenosis; 3) EUS-guided hepatico-gastrostomies (e-HG) when the drainage was guaranteed through the placement of a SEMS between the left intrahepatic duct and the stomach (see **Fig. 3**). For e-HGs either specifically-designed stents or conventional stents were used as addressed in the Definition section of the manuscript.
In the PTBD group we categorized the procedures as: 1) percutaneous antegrade stenting (p-AS) when a metal stent was advanced trans-hepatic and finally placed bypassing a stenosis; 2) percutaneous external/internal drainage (p-EID) for a trans-cutaneous, trans-hepatic, trans-papillary catheter; 3) percutaneous external drainage (p-ED) when the stenosis could not be passed and drainage was obtained through a trans-hepatic externally-placed catheter connected to a drainage bag.

Appendix 3
Clinical success was defined as: 1) the successful management of choledocholithiasis (clinical diagnosis); 2) a lowering bilirubin ≥ 25% in case of

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stenosis with elevated bilirubin (laboratory diagnosis); 3) the achievement of a desired clinical result (e.g. successful internalization of a PTBD drainage, removal of an inward migrated stent, a clinical resolution of symptoms / clinically significant reduction in inflammatory markers or cholestatic set) in case of no bilirubin elevation or unavailable serial measurement (clinical diagnosis).

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Table S1 Laboratory evaluation among technically successful procedures.

Variable	Total N = 87
Cholestasis*	
Available biochemical serial measurement, n	66
Pre-procedural elevation of bilirubin, n (%)	63 (95.5%)
Median pre-procedural bilirubin [IQR], mg/dl	7 mg/dL [3.5-13.8]
Any post-procedural reduction of bilirubin, n (%)	61/63 (96.8%)
Reduction > 25% of bilirubin, n (%)	**57/63 (90.5%)**
Reduction > 50% of bilirubin, n (%)	**44/63 (69.8%)**
Median bilirubin reduction (C.I.), mg/dL†	-4.8 mg/dl (95%CI -6.3 to -3.4)†
Median relative reduction [IQR]	64% [42.2-78]
Median time to nadir bilirubin [IQR], days	7 [5-13]
Inflammation	
Available biochemical data, n	66
Pre-procedural elevation of CRP, n (%)	62 (93.9%)
Acute post-procedural increase of CRP, n (%)	**48/63 (76.2%)**
According to adverse events status	
Patients without any clinical correlate, n (%)	22/34 (**64.7%**)§ Median increase at day 1 = +33.8 mg/dL (P = 0.0001)‡ Median increase at day 7 = N.S. [4]
Patients with mild post-procedural pain, n (%)	12/14 (**85.7%**)§ Median increase at day 1 = +37.5 mg/dL (P = 0.0093)‡ Median increase at day 7 = N.S. [4]
Patients with adverse events, n (%)	14/15 (**93.3%**)‡ Median increase at day 1 = +31.2 mg/dL (P = 0.004)‡ Median increase at day 7 = +55.6 mg/dL (P = 0.0085)‡
Radiological evaluations	
Available clinical follow-up, n	77
Post-procedural radiology, n (%)	16 (20.8%)
Asymptomatic patients,	7/16 (43.8%)

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n (%)	
Findings, n (%)	
Negative	5/16 (31.3%)
Free subdiaphragmatic air	2/16 (12.5%)
Pleuro-pulmonary involvement	9/16 (56.3%)
	6
New or increase pleural effusion	5
Basal hypoventilation	
Free fluid in Douglas	1/16
Hemoperitoneum	1/16

IQR, interquartile range; CRP, C-reactive protein; NS, not significant

*Among patients with biliary stenosis (excluding choledocolithiasis)

†Hodges-Lehmann median bilirubin reduction comparing pre-procedural and nadir bilirubin (Wilcoxon test, $P < 0.0001$).

§χ-squared test for proportions of elevation $P = 0.0607$, χ-squared test for trend $P = 0.0208$.

‡Hodges-Lehmann median difference between pre-procedural CRP and CRP at day 1 or 7 at Wilcoxon test.

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Table S2 Technical aspects among hepatico-gastrostomies.

Hepatico-gastrostomies	**N=43**
Technical success, n (%)	38 (88.4%)
Procedural length [IQR], minutes	34 [24-52]
Type of stent, n (%)	
FC-SEMS	13 (34.2%)
UC-SEMS	1 (2.2%)
PC-SEMS	1 (2.2%)
Overlapping UC (intrahepatic) + FC (transgastric)-SEMS	7 (15.6%)
HC-SEMS (Giobor)	16 (37.7%)
Diameter 8 mm	4
Diameter 10 mm	12

Variable	Purpose-specific stents (N=16)	Previous approaches (N=22)	*P* value
Clinical success, n (%)	15/16 (93.7%)	21/22 (95.5%)	0.82
Procedural length [IQR], minutes	**25 [19-31.8]**	**48 [32-64]**	**0.004 ***
Bilirubin reduction ≥ 25%, n (%)†	12/13 (92.3%)	15/18 (83.3%)	0.45
Bilirubin reduction ≥ 50%, n (%)†	8/13 (61.5%)	8/18 (44.4%)	0.36
Adverse events, n (%)	4/17 (23.5%)	7/22 (31.8%)	0.71
Stent dysfunction, n (%)	**1/15 (6.7%)**	**6/20 (30%)**	**0.09**

* Statistically significant

† Among patients with pre-procedural bilirubin elevation

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Table S3 Failures/adverse events/dysfunctions among hepatico-gastrostomies.

Age	Year	Primary Disease	Level of stenosis	AScites	Metastasis	Reasons for a transgastric approach	Isolated bile ducts	Stent model	Stent diameter	Stent length	PP Hospital stay	Death	Survival	Comment
Technical failures														
74	2018	Pancreatic cancer	Distal	0	0	Papillary inaccessible for tumor/stenosis/inflammation	N				4	0	439	Opacification and biliary cannulation, but scope issue impeding stent placement
78	2018	Cholangiocarcinoma	Hilar	0	0	Failed ERCP cannulation	Y				9	0	399	Opacification and biliary cannulation, but not enough space for stent placement
87	2019	Pancreatic cancer	Distal	0	0	Failed ERCP cannulation	N				4	1	82	GW dislocation
71	2019	Cholangiocarcinoma	Hilar	NA	NA	Failed ERCP cannulation	Y	HC Giobor / Taewoong	NA	NA	12	0	146	Extragastric stent opening + bile leak > surgery
67	2019	Benign stricture	Anastomotic	0	0	Surgery impeding access to papillary region	Y				9	0	36	Inability to puncture BD

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Clinical failures														
82	2018	Pancreatic cancer	Distal	0	0	Papillary region inaccessible for tumor/stenosis/inflammation	1	FC Wallflex / Boston Scientific	10	80		1	2	Non-lowering bilirubin + fatal adverse event, see £
74	2019	Cholangiocarcinoma	Anastomotic	1	1	Surgery impeding access to papillary region	1	HC Giobor / Taewoong	8	80	16	1	16	Non-lowering bilirubin
Adverse events [excluding mild abdominal pain]														
66	2014	Cholangiocarcinoma	Hilar	1	1	Papilla accessible but ERCP failed	1	FC Niti-S / Taewoong	10	100		1	11	Cholangitis, PP day 3
89	2016	Ampulloma	Distal	0	1	Papillary region inaccessible for tumor/stenosis/inflammation	0	HC Giobor / Taewoong	10	80		1	21	Severe abdominal pain, SDPP, requiring additional hospitalization
45	2017	Pancreatic cancer	Distal	0	1	Papillary region inaccessible for tumor/stenosis/inflammation	0	FC Wallflex / Boston Scientific	10	80	17	1	379	Cholangitis, PP day 4
59	2017	Cholangiocarcinoma	Hilar	0	0	Papilla accessible but ERCP failed	0	UC + FC Wallflex / Boston Scientific	10	60	10	1	273	Bacteremia, SDPP

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76	2018	Cholangiocarcinoma	Anastomotic	0	1	Surgery impeding access to papillary region	1	UC + FC Wallflex / Boston Scientific	10	60	1	1	138	Cholangitis, PP day 1
82£	2018	Pancreatic cancer	Distal	0	0	Papillary region inaccessible for tumor/stenosis/inflammation	0	FC Wallflex / Boston Scientific	10	80		1	2	Severe bleeding PP day 1, CT suspecting origin near the HG tract. Duodenal perforation during a previous procedure, which is likely to have played a major role in the outcome.
57	2018	Pancreatic cancer	Distal	NA	NA	Papillary region inaccessible for tumor/stenosis/inflammation	0	FC Wallflex / Boston Scientific	10	80	4	1	136	Bile leak peritonitis managed conservatively

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78	2018	Cholangiocarcinoma	Hilar	0	0	Surgery impeding access to papillary region	1	PC Wallflex / Boston Scientific	10	80	13	0	337	Cholangitis, SDPP
52	2019	Benign stricture	Anastomotic	0	0	Surgery impeding access to papillary region	0	HC Giobor / Taewoong	10	100	11	0	99	Cholangitis, PP day 0
78	2019	Pancreatic cancer	Distal	0	0	Papilla accessible but ERCP failed	0	HC Giobor / Taewoong	8	100	9	0	21	Cholangitis, PP day 1
Stent dysfunction														
50	2016	Pancreatic cancer	Distal	1	1	Surgery impeding access to papillary region	0	FC Wallflex / Boston Scientific	10	80	16	1	49	Stent obstruction PP day 42, no additional procedure
57	2017	Cholangiocarcinoma	Hilar	0	1	Surgery impeding access to papillary region	0	FC Wallflex / Boston Scientific	10	80	7	0	866	Stent obstruction PP day 424 solved by substitution of the SEMS using the same fistulous tract

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59	2017	Cholangiocarcinoma	Hilar	0	0	Papilla accessible but ERCP failed	0	UC + FC Wallflex / Boston Scientific	10	60	10	1	273	Stent obstruction PP day 140 solved by SEMS in SEMS
64	2018	Pancreatic cancer	Anastomotic	1	0	Surgery impeding access to papillary region	0	UC + FC Wallflex / Boston Scientific	10	60	8	1	167	Stent obstruction PP day 96 solved by new HG
61	2018	Ab estrinseco malignant compression	Hilar	1	0	Papilla accessible but ERCP failed	0	UC + FC Wallflex / Boston Scientific	10	60	8	1	251	Stent obstruction PP day 77 solved by new HG
78	2018	Cholangiocarcinoma	Hilar	0	0	Surgery impeding access to papillary region	1	PC Wallflex / Boston Scientific	10	80	13	0	337	Cholangitis, PP day 0 + Stent obstruction PP day 196 solved by intra-SEMS plastic placement

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75	2019	Benign stricture	Anastomotic	1	0	Surgery impeding access to papillary region	0	HC Giobor / Taewoong	8	80	7	0	57	Stent obstruction PP day 43 solved by transgastric SEMS cleaning through Dormia

SEMS, self-expanding metal stent; GW, guidewire; PP, post-procedure; HG, hepatico-gastrostomy; SDPP, same day post-procedure