PBD treatment of cancer of the head of the pancreas

Niels A. van der Gaag and Dirk J. Gouma

We thank Neoptolemos and Halloran for their critical commentary (PBD—better stents in specialized centers are needed. *Nat. Rev. Clin. Oncol.* 7, 244–246)¹ of the ongoing debate and our recent trial concerning preoperative biliary drainage (PBD).² However, we would like to clarify some misunderstandings by the authors, as well as questionable interpretations from other studies. Moreover, the commentary did not clearly present the general clinical dilemma for the physician; that is, whether to perform PBD in a patient with jaundice, suspected to have a pancreatic malignancy and eligible for surgery, but without information of underlying pathology at this stage. Our scenario analysis of surgery following PBD versus surgery alone found no benefit of routine PBD.²

Neoptolemos and Halloran commented that our study was not blinded,¹ but the nature of our trial—evaluating the consequences of an additional invasive procedure—does not allow for blinding. Initial stenting for PBD was performed mostly in district (community) hospitals and success rates did not differ significantly with those of university centers. If failure occurred, the patient was referred to a tertiary center for a second attempt or, ultimately, percutaneous transhepatic drainage (PTD). This step-up approach led to a 96% success rate for stent placement. Of note, the erroneously quoted 25% rescue PTD rate was in fact 12%. Regarding antibiotic prophylaxis, current literature does not dictate routine antibiotics for PBD through endoscopy.^{3,4}

Placement of plastic stents for PBD is common practice worldwide, owing to easy availability and low costs, and is common practice in the UK,⁵ including at the commentary authors' institution. Costly self-expanding metal stents are currently recommended for palliation, but a high level of evidence does not yet exist for their use for PBD.^{6–9} These stents might lead to a lower complication rate compared with plastic stents, but complication rates

associated with stenting will always be higher than in strategies without.

With respect to diagnostics we believe that further investigations are not indicated for patients with jaundice, who on CT scan display a lesion in the pancreatic head without metastasis and extensive vascular ingrowth. These findings will not change the treatment strategy, and these patients should always proceed to surgical exploration. In patients without a lesion, additional endoscopic ultrasound might be performed. At this stage routine diagnostic laparoscopy has limited additional value.¹⁰

Neoptolemos and Halloran claim that mortality rates of 13% and 15% are excessive.¹ However, instead of the regularly reported 30-day in-hospital mortality following resection, we employed a 120-day observation period following randomization. In this period we observed all patients, including those that were judged unresectable intraoperatively or that were not operated upon, and who died shortly after from progressive disease. Thus, the mortality we reported is entirely incomparable to the studies referred to in the commentary.^{11,12} Although our study was carried out in the setting of general practice with medium-volume and high-volume experience (the entry condition of performing at least 10 resections per year was made in an earlier study)¹³ we agree with the authors that treatment of patients with pancreatic cancer should be centralized in high-volume centers.

The claim that periampullary tumors have better interventional outcomes has no evidential grounds. On the contrary, extensive tumor growth around the papilla can be a complicating factor for the endoscopist. The non-dilated pancreatic duct in periampullary tumors, compared with pancreatic adenocarcinomas, is an established risk factor for anastomotic leakage.^{14,15} Furthermore, we performed a logistic regression analysis for the primary end point with correction for several predefined risk

factors including tumor pathology and BMI (differences between the groups were merely the consequence of randomization).

Suggestions about performing PBD in light of administration of neoadjuvant (chemoradiation) therapy, management of cholangitis or severe obstructive jaundice are in agreement with the discussion in our paper, but so far there is no evidence for these statements. We subscribe to the suggestion of Neoptolemos and Halloran that techniques that allow for a higher stent patency for PBD should be employed for these subgroups of patients, and that the statement of self-expanding metal stents as a better drainage option should be investigated. Our randomized trial has demonstrated that a PBD strategy increases complications significantly. The best option is not to postpone surgery.

Department of Surgery, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands (N. A. van der Gaag, D. J. Gouma).

Correspondence to: N. A. van der Gaag
navandergaag@gmail.com

doi:10.1038/nrclinonc.2010.45-c1

Competing interests

The authors declare no competing interests.

1. Neoptolemos, J. P. & Halloran, C. M. Surgical oncology: PBD—better stents in specialized centers are needed. *Nat. Rev. Clin. Oncol.* 7, 244–246 (2010).
2. van der Gaag, N. A. *et al.* Preoperative biliary drainage for cancer of the head of the pancreas. *N. Engl. J. Med.* 362, 129–137 (2010).
3. van den Hazel, S. J. *et al.* Piperacillin to prevent cholangitis after endoscopic retrograde cholangiopancreatography. A randomized, controlled trial. *Ann. Intern. Med.* 125, 442–447 (1996).
4. Banerjee, S. *et al.* Infection control during GI endoscopy. *Gastrointest. Endosc.* 67, 781–790 (2008).
5. Smith, R. A. *et al.* Preoperative resolution of jaundice following biliary stenting predicts more favourable early survival in resected pancreatic ductal adenocarcinoma. *Ann. Surg. Oncol.* 15, 3138–3146 (2008).
6. Adler, D. G. *et al.* ASGE guideline: the role of ERCP in diseases of the biliary tract and the pancreas. *Gastrointest. Endosc.* 62, 1–8 (2005).
7. Baron, T. H. & Kozarek, R. A. Preoperative biliary stents in pancreatic cancer—proceed with caution. *N. Engl. J. Med.* 362, 170–172 (2010).
8. Lawrence, C., Howell, D. A., Conklin, D. E., Stefan, A. M. & Martin, R. F. Delayed

pancreaticoduodenectomy for cancer patients with prior ERCP-placed, nonforeshortening, self-expanding metal stents: a positive outcome. *Gastrointest. Endosc.* **63**, 804–807 (2006).

9. Mullen, J. T. *et al.* Pancreaticoduodenectomy after placement of endobiliary metal stents. *J. Gastrointest. Surg.* **9**, 1094–1104 (2005).
10. Nieveen van Dijkum, E. J. *et al.* Laparoscopic staging and subsequent palliation in patients with peripancreatic carcinoma. *Ann. Surg.* **237**, 66–73 (2003).
11. Winter, J. M. *et al.* 1,423 pancreaticoduodenectomies for pancreatic cancer: A single-institution experience. *J. Gastrointest. Surg.* **10**, 1199–1210 (2006).
12. Balcom, J. H. 4th, Rattner, D. W., Warshaw, A. L., Chang, Y. & Fernandez-del Castillo, C. Ten-year experience with 733 pancreatic resections: changing indications, older patients, and decreasing length of hospitalization. *Arch. Surg.* **136**, 391–398 (2001).
13. van Heek, N. T. *et al.* Hospital volume and mortality after pancreatic resection: a systematic review and an evaluation of intervention in the Netherlands. *Ann. Surg.* **242**, 781–788 (2005).
14. de Castro, S. M., Busch, O. R., van Gulik, T. M., Obertop, H. & Gouma, D. J. Incidence and management of pancreatic leakage after pancreatoduodenectomy. *Br. J. Surg.* **92**, 1117–1123 (2005).
15. Pratt, W. B., Callery, M. P & Vollmer, C. M. Jr. Risk prediction for development of pancreatic fistula using the ISGPF classification scheme. *World J. Surg.* **32**, 419–428 (2008).