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Preoperative drainage in pancreatic cancer.

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ondary prevention of PTSD. We encourage the authors to continue interrogating their database to determine whether or not fentanyl and ketamine are as effective.

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No potential conflict of interest relevant to this letter was reported.

TO THE EDITOR: It seems curious that a sizable proportion of troops injured on the battlefield never received morphine or apparently any form of opioid analgesia. The article fails to offer an explanation for this finding. An analysis of the predictors for receiving morphine would be instructive with regard to the relationship between morphine administration and development of PTSD.

In addition to the proportion not receiving opioid analgesia, the relatively low morphine dosages provided raise the question of whether injured troops are getting adequate analgesia.

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Dr. Saxon reports receiving consulting fees from Reckitt Benckiser. No other potential conflict of interest relevant to this letter was reported.

THE AUTHORS REPLY: With regard to the query raised by O'Connell and colleagues as to whether morphine was associated with any adverse outcomes among patients treated at the facilities studied: no morphine-related adverse events or outcomes were reported by care providers. O'Connell and colleagues also highlight an interesting and important area for future study — whether prefacility opiate administration might affect PTSD rates. To our knowledge, there are very few comprehensive data available on the provision of pre-

hospital treatment after combat injury in Iraq; thus, it is not possible to investigate whether medications administered before arrival at treatment facilities may also have been associated with a reduction in the risk of PTSD. However, an argument based on epidemiologic principles would suggest that misclassification errors of morphine administration status would be more likely to attenuate the odds ratios observed rather than artificially inflate them.

We agree that the association between PTSD and the “fragments from blast — NOS” mechanism of injury is intriguing. But given the small number injuries in the study incurred through this mechanism, a more detailed analysis and expanded database would be required to further elucidate the relationship between PTSD and blast-related mechanisms of injury.

Schofield and colleagues bring attention to the important issue of a multimodal analgesic approach, including the use of fentanyl, ketamine, and benzodiazepines, to the care of severely injured patients. Indeed, we are initiating a study in that regard.

Saxon brings up an interesting clinical issue relating to the care of combat casualties. We agree that further studies conducted to examine clinical and injury-related predictors of morphine administration during resuscitation would be a valuable new topic of research. However, the basis of clinical decision making on the use of analgesia in the area of acute trauma care and resuscitation was outside the scope of this study.

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Preoperative Drainage in Pancreatic Cancer

TO THE EDITOR: The study by van der Gaag et al. (Jan. 14 issue)¹ comparing preoperative biliary drainage with surgery alone in patients with pancreatic cancer has some noteworthy limitations.

First, the trial design mandates a preoperative delay of 4 to 6 weeks after biliary drainage, as compared with surgery alone within 1 week. This protocol, which is based on less than persuasive

scientific evidence from studies in humans,² precludes a fair comparison of the two study groups and disregards the usually unavoidable logistic requirement for treatment delay.³ A more informative trial design would have compared study groups with both equal and achievable waiting times for surgery (e.g., 2 to 4 weeks).

Second, the study protocol did not call for systematic use of endoscopic ultrasonography, an important tool in the diagnosis and staging of pancreatic cancer.^{4,5} This omission may well have accounted for the relatively high proportion of patients undergoing surgery who ultimately proved to have either benign or unresectable disease (39%).

Finally, the authors' exclusion of patients with a bilirubin level of more than 250 μmol per liter (14.6 mg per deciliter) may have biased their results, since the excluded patients probably would have been at substantially higher risk for cholangitis than those with lower values and therefore would have stood to gain a greater benefit from biliary drainage. The exclusion of these patients would make the study's conclusions inapplicable to such patients.

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TO THE EDITOR: Van der Gaag et al. report that routine preoperative biliary drainage increased the rate of complications for patients undergoing surgery for cancer of the pancreatic head. However, several issues require discussion. First, immediate biliary drainage is needed in acute suppurative cholangitis or deep obstructive jaundice

(total bilirubin level, >15 mg per deciliter), which may lead to severe hepatic and immune dysfunction. A recent study confirmed that preoperative biliary drainage for ampullary cancer significantly reduced postoperative wound infection.¹ Second, the use of long-term biliary drainage may have contributed to stent occlusion with secondary cholangitis that could explain most drainage-related complications in this study.² Therefore, the increased complication rate may be due to routine but unnecessary preoperative biliary drainage in the majority of patients and a prolonged duration of biliary stenting. Whether selected patients with deep jaundice could benefit from short-term preoperative biliary drainage deserves further investigation.

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TO THE EDITOR: In the editorial accompanying the article by van der Gaag et al., Baron and Kozarek¹ conclude that a randomized, controlled trial should be conducted to compare preoperative biliary drainage using self-expandable metallic stents (SEMS) with surgery alone in patients with cancer of the pancreatic head. Since we have shown the superiority of covered SEMS over uncovered SEMS for unresectable malignant biliary obstruction,² it seems reasonable to consider the use of covered SEMS, rather than uncovered SEMS, as an attractive option in preoperative biliary drainage. However, on the basis of the findings of van der Gaag et al., we wonder whether a randomized, controlled trial should be performed, as suggested by Baron and Kozarek. The use of SEMS could eliminate the risk of cholangitis and surgical complications from a palliative bypass. Nevertheless, the immediate endoscopic complications (e.g., bleeding and pancreatitis), which accounted for 23% of complications related to pre-

operative biliary drainage in the study, would not have been avoided and thus might not show the superiority of preoperative biliary drainage using SEMS.

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TO THE EDITOR: Van der Gaag et al. conclude that preoperative biliary drainage in patients undergoing surgery for cancer of the head of the pancreas increases complications. Previous studies have shown that stenting is associated with a doubling in the risk of wound infection and an overall slightly increased risk of any complication.¹⁻³

Of note, the trial mandated a waiting period of 4 to 6 weeks after biliary drainage, which is not typical practice. It is unclear whether patients who underwent biliary drainage received periprocedural antibiotics. In addition, the significantly higher body-mass index in the drainage group would predict a higher complication rate.⁴ What size of biliary endoprosthesis was mandated? Size 7-French plastic stents occlude more frequently than do size 10-French plastic stents. Metallic endoprostheses occlude much less frequently, and despite statements to the contrary, they can be removed at the time of resection.

In this era of cost consciousness, should patients with obstructive jaundice and periampullary neoplasia be endoscopically manipulated? Or if imaging shows resectable periampullary neoplasia, should the patients undergo early surgery? In most cases, we favor the latter.

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TO THE EDITOR: I would like to know the rationale behind administering antibiotics routinely before surgery but leaving their use “up to local policy of the hospital’s endoscopist performing ERCP [endoscopic retrograde cholangiopancreatography],” as stated in the article by van der Gaag et al. I suggest that the failure to use antibiotic prophylaxis routinely before ERCP was a major factor increasing the risk of complications, with cholangitis representing the largest percentage (26%) of these. Whereas the use of antibiotics may not be warranted in patients in whom biliary drainage is likely to be successful, its use is warranted for patients in whom the procedure has a high likelihood to fail, such as in the clinical setting of the investigators, with success rates for initial drainage ranging from 69 to 83%. Current recommendations for the use of prophylactic antibiotics in patients with biliary obstruction who are undergoing attempted endoscopic drainage call for using drugs that are excreted through the liver, such as ceftriaxone, piperacillin, and DNA gyrase inhibitors.¹⁻³

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TO THE EDITOR: In the study by van der Gaag et al., the increased complication rate in the group

undergoing preoperative biliary drainage was from complications arising from stenting. Specifically, 30% of patients receiving stents had to have their stents changed during the 5.2-week window between stent insertion and surgery. This rate of stent replacement (for occlusion or cholangitis) within such a short period is far in excess of others' experience when using plastic stents in obstructing cancers of the pancreatic head.¹ More information should have been given about the type and size of plastic stents used. Presumably, the plastic stents used were at least 10 French in size?

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1. Moss AC, Morris E, MacMathuna P. Palliative biliary stents for obstructing pancreatic carcinoma. *Cochrane Database Syst Rev* 2006;2:CD004200.

THE AUTHORS REPLY: Dawwas et al. suggest that a comparison of equal and shorter waiting times for surgery (2 to 4 weeks) would be more informative. We evaluated the presumptive therapeutic benefit of routine biliary drainage. With respect to the optimal interval between preoperative biliary drainage and surgery, as Wang and Kao discuss, the available literature suggests that a period of at least 4 to 6 weeks of drainage is needed to reverse metabolic disorders and to yield any benefit.^{1,2} A longer period is unlikely to result in a better outcome but increases the risk of complications and unresectability. Whenever neoadjuvant therapy is scheduled or logistic hurdles arise that preclude early surgical resection, preoperative biliary drainage is indicated to bridge the time to surgery. Our study clearly shows that this strategy increases complications significantly. Approaches for avoiding such complications include performing early surgery or using techniques that allow for a higher stent patency. In response to the comments by Tsujino et al.: such higher patency is likely to be achieved with the use of SEMS that have a patency rate superior to that of plastic stents.

In response to the comments by Kennedy et al. and Mönkemüller: the standard-type plastic biliary stent that we used in our study was size 10 French. In accordance with a randomized, controlled trial conducted at our center and current

guidelines of the American Society for Gastrointestinal Endoscopy, centers in the Netherlands do not routinely administer prophylaxis for drainage in cases of obstruction of the distal bile duct. Such prophylaxis is reserved for cases with contrast filling of the bile duct but without ensuing biliary drainage or whenever incomplete drainage is anticipated in hilar strictures and primary sclerosing cholangitis.^{3,4}

We used validated computed tomographic (CT) criteria to select patients for surgical exploration. Endoscopic ultrasonography was performed selectively in patients with inconclusive findings on CT. The added value of endoscopic ultrasonography after high-quality CT to assess vascular ingrowth is limited. Most patients present with a bilirubin level below 250 μmol per liter. Higher values are likely to be associated with profound hepatic impairment, and such patients may well benefit from preoperative biliary drainage, as is our current treatment strategy.

Like Gorard, we were surprised at the high rate of stent occlusion, with or without cholangitis, in our study. A possible explanation is that our patients had malignant distal disease, and for them the surgical intent was curative, rather than only palliative. Furthermore, high-volume expert centers report lower numbers of complications than we reported, but such results do not represent usual clinical practice, which is why our multicenter design also included community centers.⁵

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THE EDITORIALISTS REPLY: We agree with Tsujino et al. that the rates of bleeding and pancreatitis that were seen in this study could offset improvement in outcome after endoscopic placement of SEMS in patients with obstructive jaundice and resectable cancer of the pancreatic head. Because preoperative drainage probably would not improve the postoperative outcome in such patients, any proposed study should be limited to those with severe pruritus when surgery is delayed, those with cholangitis, or those receiving neoadjuvant therapy. We also stated that the ERCP success and complication rates probably represent those seen in usual clinical practice. However, the complication rates were higher than expected. Size 10-French biliary stents and SEMS can be safely placed in patients with pancreatic cancer without performing biliary sphincterotomy.^{1,2} This approach would have eliminated bleeding. In addition, patients with pancreatic cancer who undergo ERCP for biliary drainage are at low risk for post-ERCP pan-

creatitis, because most of these patients are older and transient obstruction of pancreatic ductal flow caused by edema at the level of the major papilla, a main cause of post-ERCP pancreatitis, is less important, since the main pancreatic duct is already obstructed by tumor.

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Nosocomial Bacterial Meningitis

TO THE EDITOR: In their review of nosocomial bacterial meningitis, van de Beek et al. (Jan. 14 issue)¹ advocate for cerebrospinal fluid analysis as part of the diagnostic approach. We certainly agree that investigative study and empiric antimicrobial therapy should be initiated promptly when the clinical suspicion is high. However, like others,^{2,3} we have previously reported that lumbar puncture should not be used indiscriminately, particularly given the low yield in the general hospitalized population and the possibility (albeit exceedingly low) of the development of iatrogenic meningitis after the procedure.¹ Indeed, it appears that the probability of nosocomial bacterial meningitis may be defined primarily by patient history (e.g., recent head trauma, neurosurgical procedures, or immunosuppression), as supported by the authors' previous work,⁴ and lumbar puncture may be reasonably deferred in the absence of clear preexisting risk factors.

In addition, the authors neglected to mention the use of external ventricular drain catheters impregnated with antibiotics, which have been shown to lower the risk of infection significantly.⁵ Given the considerable morbidity associated with the complication of meningitis after ventricular catheter placement, these devices should be considered as part of a prevention strategy.

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TO THE EDITOR: We are concerned that van de Beek and colleagues suggest that a serum concentration of vancomycin of only 15 to 20 μg per milliliter constitutes efficient first-line therapy for nosocomial bacterial meningitis. Admittedly, these