

RFA for HCC patients within the Milan criteria in terms of overall survival.

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Reply:

We appreciate the opportunity to engage in discussion with Dr. Cho and the Korean group. The first issue is the inclusion criteria of our study.¹ We have been asked our reasoning for choosing patients conforming to the Milan criteria for liver transplantation (LT) instead of restricting our inclusion criteria to single HCC lesions less than 3 cm. The theory that radiofrequency ablation (RFA) is inferior to hepatic resection (HR) for HCC larger than 3 cm is widely supported. However this theory, like all others, needs to be based on adequate evidence. This study provides additional information on the validity of the “3 cm rule.” This study also provides data on larger diameter and multinodular lesions. We think the subgroup analyses of this study certainly address Dr. Cho’s concerns. If it is possible in future studies, it would certainly be optimal if each subgroup analysis could be separately performed with adequate samples.

Secondly, the Korean colleagues are concerned about the diversion of the remote hepatic recurrence rate of the current study compared to previous reports. In our study, the remote hepatic recurrence rate was 33% for the HR group and 50% for the RFA group (not 41% vs. 54%; see Table 5).¹ Nonetheless, they are both discordant with 70%, as Dr. Cho has mentioned. In our opinion, this discordance could be because of many reasons, not just the small sample size, including

for example: different resection maneuvers (anatomic or nonanatomic), different underlying liver diseases (approximately 40% of patients are noncirrhotic in this study), etc. As far as we know, the reported remote intrahepatic recurrence rate of HCC is actually quite variable, not only between different modalities but also between different case series.^{2–4} Thus, we can hardly agree that this diversion would influence the conclusion.

Thirdly, both the Korean and French colleagues point out that the lost-to-follow-up rate is relatively high in this study, especially in the HR group (15.7% vs. 6.1%). Although we acknowledge that the data of these lost-to-follow-up patients might have some influence on the results, it is unlikely that they would influence the significant difference in the overall survival (OS) between the HR group and the RFA group. In our experience, there are probably 3 major reasons for patients being lost to follow-up: first, death; second, cancer recurrence and then opting for another hospital; third, survival without recurrence and feeling that it is unnecessary to be followed up any longer. A sensitivity analysis can be done by assuming the extreme situation which benefits the OS of the RFA group the most: the lost patients ($n = 18$) in the HR group all died the day after their last visit and all the lost patients ($n = 7$) in the RFA continue to live healthy lives without recurrence until the end of the study. If we replace the censored data of the 25 lost patients with these assumed parameters, the difference in the OS between the 2 groups is still significant ($P = 0.003$ by log-rank test).

Finally, we admit that the current study has its limitations. As we have mentioned in the article, it is a single center, unblinded randomized trial comprised entirely of Chinese patients. Better randomized controlled trials are still needed in this field.

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Please Doctor, Resist NOTES!

To the Editor:

In the August issue of *Annals of Surgery*, Lehmann et al reported on the German experience with 551 Natural Orifice Transluminal Endoscopic Surgery (NOTES) procedures.¹ NOTES has been proposed as a new surgical innovation allowing surgical procedures via natural orifices to achieve improved surgical cosmetic results. For abdominal surgery, these potential orifices are the vagina, the mouth (through a gastrotomy), or the anus (through a rectotomy or a colostomy). The article by Lehmann et al is a report on the voluntary registry of procedures, mainly cholecystectomies, performed on women using a hybrid, rather than pure NOTES technique. Most cases presented in the report involved 10 mm transvaginal access and 5 mm umbilical trocar, with a follow-up period of 1 month.¹ Mean hospital stay for these cholecystectomies was 3.2 days. The authors reported a few intra- and postoperative complications, most of which were minor and related to the vaginal access. In our opinion, this report raises several significant issues.

First, caution has to be taken when we, surgeons, evaluate complications occurring in our own practice on a purely voluntary retrospective basis. We have a natural tendency to neglect or forget some of the complications encountered. To illustrate this, it is very intriguing that this report of 488 hybrid NOTES cholecystectomies does not describe any bile duct injury, a complication that is known to be significantly more common in “classical” laparoscopic cholecystectomies than in open cholecystectomies.² There is no reason for hybrid NOTES techniques to be safer than the standard practice, especially if bile duct opacification is not performed.³ The complications of a new procedure such as NOTES must be evaluated prospectively if a study is to be meaningful.

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In addition, I do not agree with the authors' argument that an ethical review is not necessary when proposing a NOTES technique for cholecystectomy and for publishing the results of this procedure. As the report by Lehmann et al demonstrated, this new surgical technique has specific complications that have yet to be evaluated carefully. Ethical review and patient informed consent are likely to protect not only the patients, but also the surgeons proposing these techniques. In addition, toward the end of their article, the authors mentioned that transrectal NOTES procedures have been performed on male patients upon completion of their analysis. Personally, I do not want my gallbladder removed through my colon, and I do not want to be the surgeon who will have to perform the first diverting colostomy following complicated transrectal or transcolonic NOTES, as this is bound to happen; besides the medical harm inflicted on the patient, there is no way to defend such a complication following transrectal cholecystectomy in a lawsuit.

The main question raised by the Lehmann report is the future role of (hybrid) NOTES techniques in cholecystectomies and other abdominal procedures. One of the arguments of NOTES proponents is that these techniques will be the next innovative step in surgery, just as laparoscopy revolutionized abdominal surgery 20 years ago. The advantages of laparoscopy on open surgical techniques are obvious, with less trauma and pain for the patient. Cosmetic advantages are also clear, but should be considered a less significant consequence. Laparoscopy allowed for the introduction of minimal invasiveness and fast-tracking.⁴ These advantages are far greater than the particular complications of laparoscopic techniques, such as an increased incidence of bile duct lesions for laparoscopic cholecystectomies. As a result, laparoscopy is now the standard approach for numerous abdominal procedures. What are the potential advantages of hybrid NOTES techniques, other than cosmetic, on laparoscopy? A hybrid NOTES approach, as described by Lehmann et al, requires a CO₂ pneumoperitoneum and a 5 mm trocar in the umbilicus. In Lehmann's series, mean hospitalization time was 3 days. Complications were linked to the vaginal trocar, in addition to the instrumental costs, which are somewhat higher than those of laparoscopy. As a physician and surgeon, I find the possibility of a transgastric or transcolonic approach for cholecystectomy to be even more intriguing. The necessity of a total colonic cleaning and decontamination to perform a cholecystectomy seems senseless to people who experienced bowel preparation for a colonoscopy, as I did.⁵ I do not wish to elaborate further on the issue of the cost of the bowel closing devices, and the

occurrence of tragic complications following such procedures.

Is hybrid NOTES the future of cholecystectomy? As you may have noted, I doubt it, but this technique at least needs to be carefully assessed by large, controlled, and randomized studies. Laparoscopic cholecystectomy can be safely performed with 2 mm trocars in addition to the umbilical trocar, with minimal scarring and very short hospital stays (<12 hours). Despite this, most surgeons are still using two 5 mm and one or two 10 mm trocars, and hospitalizations of 1 or 2 days. This demonstrates that, in clinical practice, surgical comfort and patient safety are superior to pure esthetic considerations. The single-incision laparoscopic surgery (SILS) may be considered a more attractive approach for the time being, but its role still needs to be assessed by careful medical and cost-effectiveness evaluation.⁶ Although awaiting the outcome of these evaluations, the surgical community must resist the increasing pressure from the surgical industry, as well as the natural surgeons' fear that they will "miss the boat" of NOTES.

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Reply:

We thank Mr. Olivier Detry for expressing his thoughts on NOTES. We think

that an open discussion about NOTES within the surgical community is very important, which was one of the aims of our report.

In general, we agree with several of the concerns that Mr. Detry raises. However, we think that some of his arguments result from misconception: Our report is not a study. We reported about data of a voluntary NOTES registry, which was established by the German Society for General and Visceral Surgery (DGAV). The DGAV cannot regulate the use of NOTES in Germany. However, the DGAV represents all visceral surgeons in Germany and therefore feels responsible for the safe introduction of NOTES. The registry was established as an instrument to monitor NOTES and to provide transparency. We think that the latter point is especially important considering the experience with the introduction of laparoscopic surgery in the 1980s.

Mr. Detry expresses concern about the thoroughness of reports in a voluntary registry, and states that there is "a natural tendency to neglect or forget some of the complications encountered." We agree that the voluntariness of a registry can be problematic. We elaborated on this topic in the discussion. In short, we feel that a voluntary design can actually improve data quality, as databases with mandatory input are usually not well accepted. The anonymous approach also encourages complication reporting. The NOTES community in Germany is still small (52 centers), and we assume that the participants are especially interested in data quality. There is also evidence that voluntary reporting, in general, does not lead to underreporting.¹ To illustrate his concerns, Mr. Detry argues that our report of 488 hybrid NOTES cholecystectomies did not contain any bile duct injuries. The frequency of common bile duct injuries in laparoscopic cholecystectomy is 0.2% to 0.5%.^{2,3} If this frequency is directly transferred to the German NOTES registry, the expected number of common bile duct injuries would be 1 to 2.4. Statistically, this number might be too small to be detected with the number of patients in our report. It is also likely that the patients in the NOTES registry depict a selected group that excludes difficult cases. Moreover, highly experienced laparoscopic surgeons usually perform NOTES procedures. In conclusion, we think that the voluntary and anonymous design of the registry actually is a strong point.

Mr. Detry also states, "NOTES must be evaluated prospectively if a study is to be meaningful." The NOTES registry has been designed prospectively and retrospective data have not been included. In general, registries offer certain advantages over randomized studies and are an eligible instrument for any procedure with inadequate evidence.⁴ We agree that NOTES must be

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