Prior Research in Measuring Financial Differences Among Surgical Specialties and Using Such Differences in Decision Making

To the Editor:

Resnick et al[1] "hypothesized that . . . significant variation in margin contribution exists between specialties." After reporting these results 5 years ago,[2] we and others showed the additional steps needed to use them in rational tactical and strategic decision making:

- Incorporate other bottlenecks such as limited intensive care unit beds.[3]
- Combine results with professional reimbursement,[4,5] to explain differences in tactical and strategic decisions between hospital administrators and medical groups.[6]
- Assess sensitivity of results to cost accounting.[7]
- Measure standard errors for the contribution margins per operating room hour.[8]
- Use the standard errors to exclude outlier patients whose data would otherwise cause spurious management decisions.[9]
- Combine the financial information with assessments of competition[10] and its impact on market share,[11] as well as shorter-term operational decisions, to form a rational tactical decision-making policy.[12]
- Combine[6] results with assessments[13,14] of what differentiates one hospital from another for strategic decision making.

Slides are available at www.FranklinDexter.net/Lectures/FinancialTalk.pdf.

The authors "question . . . how generalizable these data are to other institutions . . ." Based on our having applied these methods at more than two dozen facilities, the spread of contribution margin per OR hour among subspecialties is consistent among facilities. However, which subspecialties are highest or lowest is consistently inconsistent because of the vagaries of reimbursement versus implant costs.[6] That is why understanding how to use the observed data for good decision making is so valuable.

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Influence of Preoperative Chemotherapy on the Risk of Major Hepatectomy for Colorectal Liver Metastases

To the Editor:

Modern systemic chemotherapy agents for liver metastases from colorectal carcinoma, such as oxaliplatin and irinotecan, have been widely used in the preoperative setting for their ability to increase the cure rate in resectable tumors and to rescue some unresectable metastases to surgery, becoming standard of care in these settings.[1] Along with the benefits of such chemotherapies, several authors have reported an increased incidence of vascular changes, steatohepatitis, and the challenge of postoperative management of the patients with hepatic damage from use of these agents.[2,3] The interesting article by Karoui et al published in the January 2006 issue of *Annals of Surgery* represents a further evidence of the possible hepatotoxicity issues that modern systemic neoadjuvant chemotherapy imposes.[4]

An alternative to systemic chemotherapy for the treatment of isolated colorectal liver metastases is represented by hepatic artery infusion (HAI) chemotherapy, since the initial report by Sullivan et al in 1964.[5] Even though HAI therapy for hepatic metastases from colorectal cancer can produce high response rates and it may also be valuable to induce resectability even as second-line setting,[1] recent

advances in the systemic therapy for colorectal cancer seem to have made HAI an old-fashioned therapy.

Karoui et al[4] state that HAI chemotherapy is associated with significant pathologic abnormalities of liver parenchyma that may explain the high rate of postoperative complications observed in patients who underwent liver resection after HAI chemotherapy.

However, data concerning preoperative HAI chemotherapy are scarce. Reports of hepatic resection following preoperative HAI chemotherapy with floxuridine (FUDR) are limited to small case series.[6–9]

Several factors have restricted the wide application of HAI therapy. Intra-arterial hepatic chemotherapy with FUDR, the most used agent, is associated with a well-defined group of toxicities, including chemical hepatitis, biliary sclerosis, and gastritis,[10] and increased postoperative complications have been described in patients undergoing liver resection after HAI chemotherapy.[6] Furthermore, the need for a surgical procedure to implant the catheter into the gastroduodenal artery, the wide range of anatomic variations of hepatic vasculature, and the catheter-related complications have represented other significant limiting factors to the extensive application of HAI therapy in patients with metastatic liver disease.[10]

A number of strategies have been adopted in an attempt to overcome treatment-limiting toxicity of HAI with FUDR. The Memorial Sloan-Kettering group has been able to markedly diminish hepatic toxicity through the use of dexamethasone, as well as lowering of the FUDR dose and close monitoring of patients.[10] The description of increased postoperative complication rate following preoperative HAI chemotherapy is limited to a heterogeneous series of 14 patients with primary and metastatic tumors preoperatively treated with different systemic chemotherapy regimens and HAI with FUDR.[6] In our experience, hepatic resection following preoperative HAI with FUDR is not correlated with increased postoperative morbidity, even in elderly patients.[11]

Catheter-port systems percutaneously implanted with a transaxillary approach can overcome both the necessity of a major surgical procedure and the presence of aberrant arterial vessels.[12] In a previous study from our institution, complications of 204 patients who underwent percutaneous transaxillary implantation of a catheter for intra-arterial hepatic chemotherapy were evaluated.[13] HAI therapy could be completed in 91.2% of the patients, and the complication rate was similar to those reported in wide series of surgical implanted devices.[6] The reduced invasiveness and the reversibility of a percutaneous implant may facilitate an increase in the number of patients treated by HAI therapy and the realization of extensive clinical trials about neoadjuvant HAI chemotherapy.

The recent study of Kemeny et al suggests that HAI with FUDR may be also a valid addition to modern systemic chemotherapy regimens to render resectable previously unresectable liver metastases despite disease progression or prior systemic regimens.[14] The further development of the combination of HAI with modern systemic chemotherapy may address the concern of extrahepatic tumor progression while achieving maximal therapeutic effect in the liver.

We think that, in centers with adequate experience, there are several reasons to consider HAI chemotherapy as a valid downstaging technique for colorectal liver metastases.

First, HAI therapy with FUDR yields tumor response rates similar to modern systemic chemotherapy agents. Second, patients receiving HAI chemotherapy experience fewer side effects than systemic chemotherapy, such as myelosuppression, sensory peripheral neuropathy, and steatohepatitis, which may affect the outcome of subsequent liver resection. Third, percutaneous radiologic implantation of intra-arterial hepatic catheter may overcome the disadvantages of surgical implantation. Fourth, the application of some prophylactic measures and the close monitoring of patients may minimize the potential toxicity associated previously with HAI of FUDR.

Unless new data are available, HAI chemotherapy with FUDR may still be considered a valid strategy for downstaging of unresectable liver metastases from colorectal cancer. However, further studies are necessary to evaluate the impact of preoperative HAI chemotherapy with FUDR on the outcome of liver resection.

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Reply:

We thank Dr. Pulitanò et al for their interest in our paper. They provide general comments on the potential benefits of hepatic arterial chemotherapy as neoadjuvant treatment for unresectable liver metastases. This was not considered in our manuscript. One potential aim of the treatment of liver metastases from colorectal cancer is to render possible the resection of nonresectable lesions. Portal vein embolization increasing the size of the normal liver to be kept in place can help to remove large unilobar lesions. Local ablative therapies combined to resection allow treating in one session otherwise nonresectable lesions. But in the majority of cases, liver metastases are nonresectable because they are too numerous or too large and, in this setting, systemic chemotherapy with or without biotherapy is recommended. The question of preoperative HAI may arise in selected cases of metastases confined to the liver, well controlled by systemic chemotherapy but still unresectable and when systemic CT has to be discontinued because of some degree of toxicity. However, such a situation is probably very rare considering the wide range of effective drugs now available for intravenous use. To avoid the need of a laparotomy for catheter implantation, a percutaneous placement with a transaxillary approach is possible as suggested by Pulitanò et al, but the complication rate associated with the technique remains high. The catheter in the hepatic artery may also compromise subsequent liver resection, and this has not yet been clearly studied. Moreover, after prolonged systemic chemotherapy followed by HAI, it is reasonable to think that the risks of postoperative morbidity will be increased as compared with systemic chemotherapy alone. Finally, a very important issue is the outcome of metastases that have disappeared after chemotherapy. In many cases, these lesions are left in situ after resection. The risk of relapse is not known; and the survival benefit for the patient in these situations, although suggested by few retrospective studies, is not clear. Probably, before embarking into complex procedures, such as preoperative hepatic arterial infusion, it should be relevant to further assess the real benefit of resection of residual disease in patient who had numerous unresectable liver metastases that become amenable to resection after prolonged chemotherapy.

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Extent of Mesorectal Tumor Invasion as a Prognostic Factor After Curative Surgery for T3 Rectal Cancer Patients

To the Editor:

We read with interest the paper by Miyoshi et al.[1] We agree that T3 stage encompasses a large group of patients with depth of infiltration, ranging from just beyond the muscularis propria to mesorectal involvement without adjacent organ involvement and that this group needs to be divided further.

1. We feel that the paper is deficient in that it does not provide key information regarding the correlation between the presence and extent of mesorectal invasion and the lymph nodal status. This correlation could be established if the authors were to provide the frequency and survival figures for 4 distinct categories of patients: a) mesorectal invasion present, lymph nodes uninvolved; b) mesorectal invasion absent, lymph nodes uninvolved; c) mesorectal invasion absent, lymph nodes involved; and d) mesorectal invasion present, lymph nodes involved.
2. The findings of mesorectal invasion and its impact on survival would be further enhanced if results were to show a large number of mesorectum positive, lymph node-negative patients. On the other hand, the multivariate analysis in the paper simply establishes that both factors are independent prognostic factors.
3. What was the relationship between tumor differentiation and survival?
4. The basis and clinical significance of separation of tumors into type A and B are unclear. There appears to be no difference in the 2 groups. Further, the second data set does not show any such division.
5. We are concerned that noncontiguous involvement of the mesorectum[2–4] would be overlooked by this technique of specimen assessment. What was the frequency of occurrence of noncontiguous involvement in the series?
6. Lastly, we are concerned that surgical techniques used during the period 1960 to 1969 and 1980 to 1997 are unlikely to be identical. The concept of mesorectal invasion and standard total mesorectal excision was standardized only in the late 1980s.[4,5]

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Reply:

We have read with interest the letter from Dr. Ramesh and have considered the 6 issues he raised. We are concerned that he may have misinterpreted the data of our study.

First, the subject of our study was pathologic T3 rectal cancer, namely, tumors without mesorectal invasion (T1 or T2) were not included. If Dr. Ramesh intends to indicate that the presence of mesorectal invasion means mesorectal invasion ≥6 mm while absence of mesorectal invasion means mesorectal invasion <6 mm, we have already presented the data he asked for in Figures 4 and 5. As shown in Figure 4, patients without lymph node involvement and mesorectal invasion <6 mm (no risk factor group) had a good prognosis, while patients with lymph node involvement and mesorectal invasion ≥6 mm (2 risk factors group) had a poor prognosis. Overall survival curves of patients without lymph node involvement and invasion ≥6 mm could not be statistically separated from those of patients with lymph node involvement and invasion <6 mm (1 risk group) in these 2 data sets. Thus, we dealt with these patients as the one risk factor group (Figure 5). Moreover, we have clearly noted the correlation between lymph node status and the extent of mesorectal invasion in the Results (multivariate analysis) section. Nodal involvement had a stronger prognostic impact than the extent of mesorectal invasion in the first data set, whereas nodal involvement and extent of mesorectal invasion had nearly the same prognostic impact in the second data set. The second criticism has already been addressed in Figure 4, which demonstrated that patients with stage II tumors, in the second data set, could be categorized into 2 groups with different prognoses based on the extent of mesorectal invasion. As to Dr. Ramesh's third question, we have already illustrated the relationship between tumor differentiation and survival in Table 2.

The standard for measurement of the extent of mesorectal invasion is the outer aspect of the muscular layer. However, in cases in which this layer has been destroyed by the tumor or by extensive inflammation (type B), it is obviously not possible to identify this structure as it no longer exists. Therefore, we had to use another appropriate yardstick of measurement, ie, the straight line between the 2 break points of the muscular layer. This was the reason for 2 methods being used.

We excluded tumors invading contiguously within the muscular layer with noncontiguous tumor deposition in the mesorectum. All tumors in our study showed contiguous invasion beyond the muscular layer. The TME technique might not be performed for all patients in the second data set, although all tumors were resected with a tumor-free surgical margin. However, we are confident that this does not diminish the prognostic significance of the degree of mesorectal invasion, which has been confirmed using 2 distinct data sets.

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