Interpreting Postoperative CRP Response and HLA-DR Depression

To the Editor:

In a substudy of the LAFA (laparoscopic surgery with fast-track care) trial comparing 4 groups of patients who were randomly assigned to laparoscopic or open colectomy with or without a fast-track program with regard to duration of hospital stay, rates of morbidity and mortality, and postoperative quality of life, Veenhof et al revealed that mean levels of serum interleukin-6 and plasma C-reactive protein (CRP) level during the initial 3 days after surgery was greatest in open surgery without fast-track care and human leukocyte antigen (HLA)-DR expression on the surface of monocytes was highest in the LAFA group. Veenhof et al suggested that a better preserved immune competence and a lesser surgical stress response associated with laparoscopic fast-track surgery led to earlier postoperative recovery and shorter hospital stay, but sufficient evidence for their suggestion may be lacking. In the LAFA trial, primary outcome of median total hospital stay in the laparoscopic fast-track surgery group was 5 days, which was shorter than 6 days in the standard laparoscopic group and 7 days in the open group with or without fast-track care. Major postoperative complications prolong hospital stay after colorectal surgery. In the LAFA trial, secondary outcome such as in-hospital morbidity and mortality did not differ among the groups on the analysis of variance. In multiple logistic regression analysis, however, laparoscopic surgery yielded a marginal benefit of reducing overall and major morbidity. When looking at this study by Veenhof et al., there was no statistical difference in morbidity rates among the groups on the analysis of variance test but multivariate analysis was not performed.

HLA-DR that is expressed on monocytes, macrophages, and dendritic cells is a crucial molecule for the presentation of antigen to lymphocytes and the initiation of adaptive immune response. Earlier studies suggested the correlation of HLA-DR depression with the development of postoperative infections, and a recent study demonstrated that failure of recovery from HLA-DR depression rather than the degree of HLA-DR depression in the first postoperative week was predictive for the development of postoperative pneumonia after lung transplantation in children. A more recent study raised questions about the clinical utility of monocyte HLA-DR expression as an early predictor of postoperative complications, because low-risk operations such as knee and hip arthroplasty led to a substantial degree of monocyte HLA-DR reduction without postoperative complications. Taken together, it remains uncertain whether transient moderate reduction of HLA-DR expression in early postoperative course is secondary to a global defect in monocyte function or an unhelpful response to surgery. CRP, which was named because of its reactivity with the residues of C polysaccharide of Streptococcus pneumoniae, constitutes a genetically ancient and highly conserved family of cyclic oligomeric proteins that function against bacterial and fungal infections in mammals, amphibians, fish, and the horseshoe crab. Measurement of circulating human CRP helps in diagnosing infectious and inflammatory diseases and monitoring the response to therapy, but the clinical effectiveness of CRP measurement in early postoperative period for predicting operative outcomes has not been confirmed. It is difficult to determine whether rising CRP in this period is a physiologic response to surgical insults or mirrors developing complications. In response to surgery, de novo hepatic synthesis of CRP starts very rapidly, and blood concentrations peak around 48 hours after surgery. As the half-life of circulating CRP is estimated to be 48 hours irrespective of conditions, mean CRP value for the initial 3 days after surgery could reflect the intensity of surgical trauma and very early complications associated with surgery. The values of CRP in the fourth and fifth postoperative days were more predictive for subsequent infective complications than those measured during the initial 3 days after surgery in patients who underwent elective colorectal resection. Therefore, it would be interesting to analyze the effect of the levels of HLA-DR expression and CRP on the development of complications using a multiple logistic regression model, in which laparoscopic approach, fast-track care, and the American Society of Anesthesiologists score will be also entered as a factor possibly responsible for postoperative complications.

Tetsuji Fujita, MD
Department of Surgery
Jikei University School of Medicine
Tokyo, Japan

REFERENCES