
Sites of first distant recurrence in resected non-small-cell lung cancer

To the Editor:

I read with interest the article by Yano and associates.1 The authors hypothesize that the venous drainage of mediastinal lymph nodes is to the superior vena cava and that this may increase the likelihood of pulmonary metastasis in patients with N2 lung cancer. This proposed mechanism of metastatic spread is not present in patients with N0 lung cancer; therefore a different pattern of distant failure is anticipated. The hypothesis is fascinating, but the authors' data are insufficient to justify its acceptance.

The lung was the first site of distant recurrence in 10 of 52 patients with N0 disease and 12 of 40 with N2 disease. Although my knowledge of statistics is limited, a simple $\chi^2$ test to compare the frequency of lung metastasis in the two groups would appear to be appropriate. This test gives a $p$ value of 0.23 ($\chi^2 = 1.44$). The authors state that the overall pattern of distant metastasis was different between patients with N0 disease and those with N2 disease ($p = 0.044$). Although their statement is undoubtedly true, the difference is probably a reflection of the higher incidence of brain metastasis in the N0 group ($p < 0.013$, $\chi^2 = 6.14$). A significant difference in the prevalence of brain metastasis does not necessarily support the authors' hypothesis of pulmonary metastatic spread from mediastinal lymph nodes.

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REFERENCE


Early production of interleukin-10 during normothermic cardiopulmonary bypass

To the Editor:

Cardiopulmonary bypass (CPB) is known to cause a systemic inflammatory response associated with an increased production of proinflammatory cytokines (interleukin-1 [IL-1], IL-6, and IL-8).1,2 Several studies suggest that IL-10 is an important factor in the down-regulation of inflammatory responses, in particular by inhibiting in vitro proinflammatory cytokine synthesis by neutrophils (PMN) and monocytes.3 We hypothesized that IL-10 might be produced during CPB and could represent a regulatory mechanism controlling monocyte/PMN activation in vivo. We therefore measured plasma levels of IL-10 in comparison with that of IL-6 and IL-8 in patients undergoing cardiac operations with normothermic CPB.

Eight patients, 47.8 ± 8.9 years of age (mean standard error of the mean), were studied. Patients with corticosteroid therapy or suspected infectious disease were excluded. Anesthesia and CPB management were performed as previously described.2 Mean CPB and aortic clamping durations were 115 ± 9 and 89 ± 8 minutes, respectively (mean ± standard error of the mean). Serum blood samples were withdrawn from the radial artery catheter before sternotomy (T0), at the onset of CPB (H0), and at intervals of 1, 2, 4, 6, 10, and 24 hours (H1 to H24) after the onset of CPB. Blood samples were collected into sterile vacuum tubes with ethylenediaminetetraacetic acid, immediately centrifuged, and stored at −70°C. We measured IL-10 using an enzyme-link immunosorbent assay that is specific for human IL-10 (EASIA Medigenix, Fleurus, Belgium) and IL-6 and IL-8 by enzyme-linked immunosorbent assays from Amersham (Biotrak, les Ulis, France).

As shown in Fig. 1, whereas IL-10 was undetectable in any of the plasma samples at T0 and H0, plasma IL-10 levels rose in all of the patients as early as 1 hour after the onset of CPB, peaked either at H1 or H2 (H1, 76.2 ± 20 pg/ml; H2, 73.5 ± 24.8 pg/ml; mean ± standard error of the mean; $p = 0.01$ versus H0 by Wilcoxon's matched-paired test), and decreased at H4 (23.6 ± 10 pg/ml). IL-6 and IL-8 levels peaked at 4 and 2 hours, respectively, after the onset of CPB. By contrast with the strong posit
correlation observed between plasma IL-6 and IL-8 concentrations ($p = 0.91; p = 0.02$, Spearman rank order test), the level of IL-10 production was unrelated to the levels of IL-8 and IL-6.

Our results show that CPB causes the rapid and transient release of IL-10. The differences in kinetics and levels of production between IL-10 and IL-6 and IL-8 suggest different immunoregulatory mechanisms involved in their secretion. The in vivo kinetics of IL-10 during CPB are similar to those observed in experimental murine endotoxemia after lipopolysaccharide challenge. These kinetics contrast with in vitro data showing that IL-10 is produced rather late after lipopolysaccharide stimulation of human monocytes and suggest that other cells could be involved in the release of IL-10 in vivo. The cellular source(s) of IL-10 and the nature of stimuli leading to IL-10 release remain to be determined. We concluded that CPB induced an early IL-10 secretion. Further studies are required to determine whether this IL-10 release plays a beneficial role, by reducing the ischemia-reperfusion inflammatory response, or a detrimental role, by decreasing the cellular immune response.

REFERENCES

Intraoperative use of end-tidal carbon dioxide tension to assess cardiac output
To the Editor:

We read with interest the letter by Feng and Singh\(^1\) on the intraoperative monitoring of end-tidal carbon dioxide tension ($\text{PetCO}_2$) to assess cardiac output during weaning from cardiopulmonary bypass (CPB). The authors invited comment from those who might have made similar observations.

We have observed for some time that $\text{PetCO}_2$ is a good indicator of cardiac performance during weaning from CPB. It is our practice to monitor and record $\text{PetCO}_2$ continuously in the prebypass period, adjusting minute volume and tidal volume to achieve a $\text{PetCO}_2$ of approximately 4 kPa (30 mm Hg) before bypass. On reinstitution of ventilation and reperfusion of the lungs, we set the ventilator to deliver the same minute volume and tidal volume as before bypass. In the absence of major metabolic changes or a major change in dead space, either of which we believe occurs rarely, $\text{PetCO}_2$ will directly reflect carbon dioxide, as explained by Feng and Singh. In our experience patients tend to fall into one of three groups. The first group comprises those in whom the $\text{PetCO}_2$ level is similar to that recorded before CPB. These patients generally are able to be weaned readily from CPB with minimal additional volume requirement and without recourse to inotropic agents or assist devices.

The second group demonstrates an initial $\text{PetCO}_2$ level lower than that recorded before CPB, but this gradually returns to the prebypass level. These patients appear to commonly require preload augmentation before being successfully weaned. Last is a group that has persistent low $\text{PetCO}_2$ levels. These patients will commonly require more volume and often require inotropic support or occasionally assist devices to be weaned successfully. We have a very low threshold for instituting inotropic support in patients who have low $\text{PetCO}_2$ during weaning from CPB despite adequate preload and satisfactory heart rate and rhythm.

At present, because we do not routinely monitor intraoperative cardiac output, we have not objectively confirmed the clinical impression that we have described. We intend to study the matter in detail later this year.

REFERENCE