4. Schilling Eleftheriadis
3. Hau
2. Total using either above).

1.92 Omentum
0.17 Subcutis
1.58 Kidney
0.67 Liver
2.50 Omentum
2.75 Scrotal fat
Total tumor load

31 Letters to the Editor

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Table 3 (Revised). SOLID TUMOR MODEL: RESULTS USING THE MANNE-WHITNEY TEST

<table>
<thead>
<tr>
<th>Abdominal Site</th>
<th>CO2 (n = 8)</th>
<th>Gasless (n = 8)</th>
<th>Open (n = 8)</th>
<th>p1 CO2 vs. Gasless</th>
<th>p2 CO2 vs. Open</th>
<th>p3 Gasless vs. Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>3.00 ± 0.00</td>
<td>3.25 ± 0.46</td>
<td>3.00 ± 0.00</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Liver</td>
<td>2.50 ± 0.53</td>
<td>2.63 ± 0.52</td>
<td>2.75 ± 0.71</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Omentum</td>
<td>2.50 ± 0.93</td>
<td>1.36 ± 0.52</td>
<td>2.38 ± 0.52</td>
<td>&lt;0.02</td>
<td>NS</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>2.75 ± 0.46</td>
<td>1.25 ± 0.46</td>
<td>2.50 ± 0.76</td>
<td>&lt;0.001</td>
<td>NS</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Scrotal fat</td>
<td>2.75 ± 1.16</td>
<td>2.25 ± 0.46</td>
<td>2.75 ± 0.71</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Total tumor load</td>
<td>13.50 ± 1.2</td>
<td>10.76 ± 1.04</td>
<td>13.13 ± 1.20</td>
<td>&lt;0.001</td>
<td>NS</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

NS = not significant.

Table 4 (Revised). CELL SEEDING MODEL: RESULTS USING THE MANNE-WHITNEY TEST

<table>
<thead>
<tr>
<th>Abdominal Site</th>
<th>CO2 (n = 12)</th>
<th>Gasless (n = 12)</th>
<th>Open (n = 12)</th>
<th>p1 CO2 vs. Gasless</th>
<th>p2 CO2 vs. Open</th>
<th>p3 Gasless vs. Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneum</td>
<td>0.83 ± 0.72</td>
<td>0.00 ± 0.00</td>
<td>1.46 ± 0.78</td>
<td>&lt;0.001</td>
<td>&lt;0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subcutis</td>
<td>0.17 ± 0.39</td>
<td>0.00 ± 0.00</td>
<td>1.25 ± 1.08</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Kidney</td>
<td>1.58 ± 0.63</td>
<td>1.25 ± 0.58</td>
<td>1.96 ± 1.10</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Liver</td>
<td>0.67 ± 0.49</td>
<td>0.33 ± 0.49</td>
<td>1.13 ± 0.80</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Omentum</td>
<td>1.92 ± 0.19</td>
<td>0.58 ± 0.47</td>
<td>2.46 ± 1.18</td>
<td>&lt;0.001</td>
<td>NS</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>1.33 ± 0.78</td>
<td>1.58 ± 0.36</td>
<td>1.79 ± 1.47</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Scrotal fat</td>
<td>1.50 ± 0.96</td>
<td>0.50 ± 0.60</td>
<td>1.92 ± 1.08</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total tumor load</td>
<td>8.00 ± 1.81</td>
<td>4.25 ± 1.41</td>
<td>11.79 ± 3.63</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

NS = not significant.

(ANOVA) because our groups were relatively small. However, the principles of ANOVA are illustrated in Altman’s standard statistical textbook in three groups consisting of eight, nine, and five patients; hence, ANOVA may well be valid in small groups. Another reason to perform a nonparametric test would be that our data contained an ordering but were possibly not really continuous and normally distributed. We therefore conducted the Mann–Whitney test. The results for Tables 1 and 2 were identical to our initial results obtained with ANOVA. Results for Tables 3 and 4 were slightly different and are shown with amendments from the original tables in bold (see revised tables above). It is clear that the earlier conclusions remain unchanged, using either ANOVA or the nonparametric Mann–Whitney test.


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Dear Editor:

In their recent paper, Cox et al. describe a previous cerebral embolism as an absolute indication for surgery, their apparent reasoning being that anticoagulation does not protect these patients from a second stroke. I think this overlooks the strong evidence from the European Atrial Fibrillation Trial, which included 1007 patients with previous cerebral events and followed them for a mean of 2.3 years. In this randomized controlled trial, anticoagulation treatment reduced the annual rate of stroke from 12% in the placebo group to 4% (hazard ratio,
0.34; 95% confidence intervals, 0.20 to 0.57). The studies referred to by Cox et al. were not designed to give, and were not able to give, specific information on this relatively common group of patients in atrial fibrillation who have already had a thromboembolic event.

It is clearly vital for any surgeon considering embarking on such a major operation as the Maze procedure to be aware of other highly effective alternative treatments in preventing future strokes.

References


DR. STEPHEN MORGAN

Authors’ Reply:

The statement in question in our September 1996 article reads as follows: “Documented cerebral thromboembolism in a patient with paroxysmal or chronic atrial fibrillation, in the absence of other demonstrable etiologies, is considered an absolute indication for surgery because anticoagulation does not protect such patients from a second stroke.” Dr. Morgan is correct in pointing out that the studies we referenced were not designed to answer the specific question of protection against second strokes and that a better reference would have been the 1993 Lancet article describing the observations on this point made by the European Atrial Fibrillation Study Group. However, we suggest that this change in the statement’s reference does not change the statement’s accuracy.

In the three studies we referenced, warfarin anticoagulation decreased the incidence of strokes associated with atrial fibrillation by 51%, 81%, and 86%, respectively. This means that the absolute number of strokes that occur in the United States each year due to atrial fibrillation can be decreased from approximately 150,000 to approximately 45,000 as a result of anticoagulation (using a median reduction figure for the three studies of 70%). Despite the fact that 45,000 American citizens per year will still have strokes due to atrial fibrillation, even though they are fully anticoagulated, physicians frequently and incorrectly imply to their patients that anticoagulation protects them from the threat of stroke associated with atrial fibrillation. Indeed, the closing statement in Dr. Morgan’s letter includes the phrase “other highly effective alternative treatments in preventing future strokes” [italics added].

As pointed out by Dr. Morgan, the randomized European study demonstrated that the decrease in the incidence of second strokes by anticoagulation achieved statistical significance. Much like the example used above for first-time strokes, however, the inference seems to be that this reduction in the incidence of second strokes associated with atrial fibrillation is tantamount to abolishing the problem entirely. However, we again point out that 4% of the patients who were anticoagulated still suffered a second stroke. That represents 1800 people per year in the United States alone (4% of 45,000), a not insignificant number. Thus, we believe that it is misleading to indicate to patients who have had a previous stroke and are now anticoagulated that they are protected against a second stroke simply because they are anticoagulated.

To decrease the incidence of stroke in such patients to 0%, it is necessary to abolish the atrial fibrillation, reestablish normal atrioventricular synchrony, and restore atrial transport function. Currently, there are only two ways to accomplish those three goals: successful medical therapy and the Maze procedure. As noted in Table 1 of our report, 44 patients in our series were operated on for the primary indication of having had a previous thromboembolic event. Many of those patients had suffered severe strokes; 1 patient had had 5 separate embolic strokes in the 2 weeks before surgery. That same patient had an embolism to the right coronary artery, causing a large inferior myocardial infarction. Another had suffered an embolism to the superior mesenteric artery. Another had suffered multiple embolic strokes to both sides of the brain during the 2 months before surgery. After surgery, despite no anticoagulation after 3 months, those 44 patients combined have experienced only two mild transient ischemic attacks and no strokes.

It is probably fair to say that our statement regarding previous strokes being an absolute indication for surgery is overstated in that it is not an absolute indication. However, we stand by our assertion that anticoagulation does not protect a patient against a second stroke. We have pointed out in many previous, more detailed reports that we have never considered the threat of a stroke (i.e., a patient’s concern that he may have a stroke simply because he has atrial fibrillation) to be an indication for performing the Maze procedure. However, if a patient has already demonstrated that he or she is capable of having a stroke due to atrial fibrillation, we consider that factor to be a strong determinant of our willingness to offer him or her the Maze procedure, regardless of anticoagulant status. Our rationale is that anticoagulation does not protect against a second stroke; it only decreases the incidence of a second stroke. That rationale is confirmed by the 4% incidence of stroke in the anticoagulated patients who made up the treatment arm of the European study.

References


