IMPS (Intact Months of Patient Survival): An Analysis of the Results of Carotid Endarterectomy

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SUMMARY The literature on carotid surgery for lesions appropriate to prior episodes of ischemia has been reviewed. Only one randomized study and six non-controlled reports give useful data (this despite more than thirty years of surgical activity in this field). When analyzed by the IMPS (intact months of patient survival) criterion, the randomized study failed to show benefit from surgery. This failure can be attributed to a high (35%) operative stroke and death rate. That sufficiently low operative stroke and death rates are readily achievable is not clear, however, only two of six relevant non-controlled series reported in the literature had operative stroke and death rates below the 10.4% level calculated as necessary for a "break-even" situation. Three of the six non-controlled series contain sufficient follow-up data to permit IMPS comparison against the "standard" of the control group of the randomized study. Against this "standard" only one of the three non-controlled studies would have "shown benefit" from surgery. Barnett, Plum, and Walton have called for audits of endarterectomy results in institutions in which such surgery is "standard" only one of the three non-controlled studies would have "shown benefit" from surgery. It is suggested that such audits be done by the IMPS method, which gives appropriate weight to the effects of operative, as well as of long-term follow-up, strokes and deaths.

Since Warlow submitted his paper, Shaw et al have published a controlled study (to which Warlow alluded in a footnote) of carotid surgery for TIA and minor stroke. Although this study is small (total of 41 patients), it has several virtues: all patients were randomized for surgically treatable stenoses in carotid arteries relevant to their symptoms; much detail was provided; and mean follow-up was long (greater than six years).

I herein review the results of Shaw et al and of six noncontrolled studies. Relevant data from these seven reports are summarized in table 1. These seven reports are the only ones in the literature which meet the following rigorous criterion: they specify that they report the results of surgery on carotid arteries in whose territory TIA (transient ischemic attack), RIND (reversible ischemic neurologic deficit), or minor stroke had occurred.

Reports on Carotid Endarterectomy

Shaw recently published a detailed review on endarterectomy. It was his aim to focus on the results of surgery on carotid arteries in whose territory TIA had occurred. As he indicated, however, only one randomized study devoted to surgery for TIA had been reported at the time he undertook his analysis. In the report of that study, the outcome of the patients who had had carotid TIA cannot be separated from the outcome of the approximately 46% who had had vertebral TIA only.

This Communication has three purposes:

1. To review the published results of carotid endarterectomy on vessels in whose territory TIA (transient ischemic attack), RIND (reversible ischemic neurologic deficit), or minor stroke had occurred.

2. To analyze these results by the IMPS (intact months of patient survival) method.

3. To suggest the applicability of the IMPS analysis for the performance of institutional audits of the safety and efficacy of endarterectomy, as proposed by Barnett, Plum, and Walton.¹

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(There are, of course, many other reports on surgery, but in those other reports data of the sort described above are either inextricably mixed with, or not specified as isolated from, results of surgery on patients with no symptoms, with symptoms in one vascular territory but surgery in another territory, with surgery on vertebral or subclavian arteries, with surgery after major stroke, etc.)

IMPS Analysis

Background

Warlow stated that the proper criterion for evaluating endarterectomy results is the subsequent duration of surgical or nonsurgical tests for transient ischemic attacks and cervical carotid artery lesions. JAMA 211:1993, 1970


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of survival free of stroke. He did not actually analyze the available results in such a manner; the life-table data necessary for accurate analysis were, as he indicated, not routinely published in the literature.

I herein employ a simple method, which can be applied to data of reports lacking life-table analyses, for estimating the effect of endarterectomy on the duration of survival free of stroke. This is the IMPS (intact months of patient survival) method.12

The key to the IMPS method is the IMPS ratio. For a population followed for a given period, the IMPS ratio is the ratio between the total patient-months of intact survival time actually enjoyed by the cohort and the maximum amount which the cohort would have enjoyed had no one died or suffered stroke during the observation period. For instance: suppose that 100 patients are followed for a year. If there are no strokes or deaths, then the cohort enjoys 100 x 12 = 1200 patient-months of intact survival for the year. Suppose, however, that ten deaths occur at the end of four months and ten strokes occur at the end of eight months, while the other 80 patients are intact at one year. For this situation there are (10 x 4) + (10 x 8) + (80 x 12) = 1080 intact months of patient survival for the year. The IMPS ratio is then 1080/1200 = 0.9.

It will be recognized that the above can be given graphic representation, as in figure 1a. Here the proportion, rather than the absolute number, of patients surviving intact is given on the ordinate. The IMPS ratio can then be conveniently considered as the ratio between the area under the step-curve and the area of the entire graph. The area under the step-curve (the sum of the areas of the three broad columns defined by the three steps) is (1.0) (4) + (0.9) (4) + (0.8) (4) = 10.8. The area of the entire graph is (1.0) (12) = 12. The IMPS ratio is 10.8/12 = 0.9.

With respect to the form of the curve, it should be noted that a slope (see fig. 1b) can substitute for a step-curve in IMPS ratio calculations, if the end-point events are distributed uniformly with respect to time. For figure 1b, the area under the curve is (1.0 + 0.8) x (12) (0.5) = 10.8 (12) (0.5) = 10.8, and the area of the entire graph is (1.0) (12) = 12; the IMPS ratio is 10.8/12 = 0.9, as before.

It will be noted that for figure 1B the calculations could have been simplified; one need merely take one-half of the sum of the initial ordinate value (1.0) and the final ordinate value (0.8): (1.0 + 0.8) (0.5) = 0.9.
INTACT SURVIVAL AFTER CAROTID ENDARTERECTOMY

1.0
0.8
0.6
0.4
0.2
0
0 4 8 12
Months of Cohort Follow-Up

Proportion of Patients Who Have Not Died or Had a Stroke

The simplification derives from the disappearance of the time unit, and all other units, from the results of a ratio calculation. It will also be noted that visually the IMPS ratio is "the area under the curve of intact survival".

The Results of the IMPS Analysis of Shaw et al

It will be seen from Table 1 that the 20 surgical patients of Shaw et al suffered 7 strokes and deaths in the operative period (during, and within one month after, surgery). There were 6 strokes and deaths among the intact survivors of surgery during a mean follow-up period of 77 months after the first month. For the 21 control patients the analogous figures were zero events in the first month, and 15 strokes and deaths in the 72.2 month mean follow-up period after the first month. With adjustment of the surgical late follow-up period from 77 months to 72.2 months, the total of all strokes + deaths becomes 7 + (6) (72.2)/77 = 12.63 for the surgical cohort, a stroke + death rate of 12.63/20 = 0.631 for 73.2 months. For the control cohort the stroke + death rate is 15/21 = 0.714 for 73.2 months.

The results (0.631 versus 0.714) make surgery look better than non-surgical care (questions of statistical significance for sample size aside) as of 73.2 months. However, when the results are presented graphically, as in figure 2a (assumptions: the events of the first month are all assigned to zero time; all other events are distributed uniformly over the next 73.2 months), it will be seen that the area under the surgical curve is less than that under the nonsurgical curve. The relative numerical values for these areas (the IMPS ratios, calculated as described above in the discussion of fig. 1b) are 0.510 for surgery and 0.643 for non-surgical care. The surgical cohort thus had a less favorable outcome than the control cohort by the criterion of intact months of patient survival.

Questions Arising from Shaw et al IMPS Analysis

It will be noted from table 2 that the annual stroke and death rate among the patients of Shaw et al during long-term follow-up after the first month was lower after surgery (mean rate of 7.2% per year) than for non-surgical care (mean rate of 11.9% per year). It also has been noted that a smaller proportion of surgical patients (0.631) suffered stroke or death than did non-surgical patients (0.714) during the (adjusted) total observation period of 73.2 months.

Nevertheless, surgery failed to benefit the operated cohort in terms of duration of intact survival (as quantitatively estimated by IMPS ratio analysis). The reason, as figure 2a makes clear, is the burden of the 35%
operative stroke death rate; the protection conferred upon the intact survivors of surgery was still not great enough to have permitted the surgical cohort to "catch up" with the control cohort as of 73.2 months: the area under the surgical curve (reflecting the IMPS ratio) is still less than the area under the control curve, even though the curves have crossed.

What if the operative stroke and death rate had been lower than 35%? Could the surgical cohort have "broken even"? IMPS analysis gives an answer. At an operative stroke + death rate of 10.4%, and with no change in the stroke + death rate during follow-up, the surgical cohort would have "broken even" with the control cohort at 73.2 months by the IMPS ratio criterion. Figure 2b, in which the area under the surgical curve has been made to equal the area under the control curve, gives graphic representation to this "what if . . . " analysis. One could speculate that it is unreasonable to expect no change in the stroke and death rate in follow-up in such circumstances. For instance, it might be that patients at more than "average" risk during surgery would have more than an average chance of stroke or death in follow-up after surviving surgery intact. There are no data with which to discuss this issue meaningfully.

Questions Arising from IMPS Analysis of Non-Controlled Results

In the absence of controls one has no direct way of defining how surgery influenced the over-all outcomes among the patients of the six non-randomized cohorts. By reasoning similar to that used in the "what if . . . " analysis above, however, one can define the "natural history" outcomes against which surgery would have "broken even" in the three studies which provided follow-up as well as operative data. Thus (see table 3), one cohort would have broken even against a control cohort having an annual stroke + death rate of 6.2%. The other two would have broken even against a control cohort having an annual stroke + death rate of 6.2%. The other two would have broken even against a control cohort having an annual stroke + death rate of 6.2%.

Interpretations

A rigorous interpretation of the above results is simple: in the one controlled study, surgery failed; therefore there is no reason to recommend carotid endarterectomy on a vessel in whose territory ischemia has occurred.

As has been pointed out, however, theoretically the Shaw surgical cohort could have "broken even" had the operative stroke death rate been 10.4%, and could
Patient Survival) Ratio Calculations

The initial ordinate value is the proportion of patients intact after the end of the study. The difference is therefore not statistically significant by the usual minimal significant difference (0.20) for 1 degree of freedom and the value of 1.23: p_{\text{calculated}} > 0.05 (0.05) standard.

Surgical: follow-up adjusted to 73.2 months

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean annual stroke and death rate after operative period</th>
<th>Total rate for all strokes and deaths</th>
<th>IMPS ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shaw</td>
<td>Operation: 0.350, Control: 0.000</td>
<td>0.361</td>
<td>0.510</td>
</tr>
<tr>
<td></td>
<td>(Adjusted to 73.2 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surgical: 0.219, Control: 0.072</td>
<td>0.714</td>
<td>0.643</td>
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<tr>
<td></td>
<td>(As of end of study)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>0.040</td>
<td>0.331</td>
<td>0.814</td>
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</tbody>
</table>

For the calculation of the IMPS ratio it has been assumed that the data can be graphed as in figure 1b. The IMPS ratio is then one-half the sum of the initial ordinate value and the final ordinate value. The initial ordinate value is the proportion of patients intact after the operative or early period. The final ordinate value is the proportion intact at the end of the study. Graphing data as described above is, of course, an approximation. A more accurate way to derive the IMPS ratio would be to calculate the areas under a step-curve: either one reflecting the specific outcome of each patient if all patients had been followed for a uniform period, or one constructed from life-table data if there had been withdrawals or non-uniform durations of follow-up (see fig. 1a for a hypothetical step-curve). Such data are not available in the reports herein reviewed. For statistical analysis when such data are available, see Peto et al.11

What if one looked at relatively, rather than absolutely, intact survival? Suppose one considered the quality of life as a function of the severity and duration of disability after a non-fatal stroke. Conceivably post-surgical strokes might be less severe than control strokes. This must remain as speculation, however; no useful data are available.

In reviewing the above, it is important to recognize
that the “rigorous” rejection of surgery depends on only one controlled study covering 41 patients. However, it must also be recognized that any claim for surgery must be based on the immediate operative results of only six, and the follow-up results of only three, non-controlled series, as interpreted by the weak “historical control” method. It should be recognized that the basis for the “historical control” analysis is only the 21 control patients of the randomized study, there being no other report of patients accepted for surgery but treated non-surgically. It should be emphasized that these seven studies are the only studies germane to the question of relevant vessel surgery which are available in the literature after thirty years of the performance of carotid endarterectomy.

The Use of IMPS Analysis for Institutional Audits

Barnett, Plum and Walton have expressed uncertainty that carotid endarterectomy can be accepted as a method for preventing stroke. They look forward to a large controlled trial to resolve the issue. Until such a trial is reported, they recommend that institutions audit non-controlled endarterectomy results, and that institutions with unsatisfactory results discontinue surgery.

Clearly such an audit must include the stroke + death rate from the surgical procedures (Barnett, Plum and Walton also recommend the inclusion of arteriographic morbidity and mortality). The audit must include as well the follow-up stroke and death rates among the intact survivors of surgery. These combined data would then be judged against a “model” of the expected “natural history” of such patients in the absence of surgery.

It is obvious from the present figure 2a that the judging of observed results against the “model” should not consist merely of the comparing of total strokes and deaths as of the end of the period of observation. Such an analysis would fail to give appropriate weight to the effect of the operative strokes + death: a late stroke, such as one occurring six years after entry, and an early stroke (e.g., during surgery) are clearly not “equal” events, either for the individual or for the cohort.

The appropriate way to conduct such an audit would be by IMPS analysis. An IMPS ratio for the institution’s results would be determined (preferably from life-table data: the area under an actuarially constructed curve of results). This would then be compared to a “control IMPS ratio” estimated by the auditors to be “reasonable” for the surgical cohort being audited.

Acknowledgments

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References

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