

SELECTED ABSTRACTS

Influence of smoking on aneurysm recurrence after endovascular treatment of cerebrovascular aneurysms

John Futchko, Jordan Starr, Darryl Lau, Matthew R. Leach, Christopher Roark, Aditya S. Pandey, B. Gregory Thompson
J Neurosurg. 2018 Apr;128(4):992-998

Abstract

Objective

Smoking is a known risk factor for aneurysm development and aneurysmal subarachnoid hemorrhage, as well as subsequent vasospasm in both untreated individuals and patients who have undergone surgical clipping of cerebrovascular aneurysms. However, there is a lack of data in the current scientific literature about the long-term effects that smoking has on the integrity of endovascular repairs of cerebral aneurysms. This study was designed to determine if any smoking history increased the risk of poorer outcomes and/or aneurysm recurrence in patients who have had endovascular repair of cerebral aneurysms.

Method

The authors retrospectively analyzed the medical records of patients admitted to the University of Michigan Health System from January 1999 to December 2011 with coiled aneurysms and angiography, CT angiography or MR angiography followup. Patients were identified and organized based on many criteria including age, sex, smoking history, aneurysm recurrence, aneurysm location, and Hunt and Hess grade. Analysis was targeted to the patient population with a history of smoking. Bivariate chi-square tests were used to analyze the association between a positive smoking history and documented aneurysm recurrence and were adjusted for potential confounders by fitting multivariate logistic regression models of recurrence.

Result

A total of 247 patients who had undergone endovascular treatment of 296 documented cerebral aneurysms were included in this study. The recurrence rate among all patients treated with endovascular repair was 24.3%, and the average time to the most recent follow-up imaging studies was 1.62 years. Smokers accounted for 232 aneurysms and were followed up for an average of 1.57 years, with a recurrence rate of 26.3%. Never smokers accounted for the remaining 64 aneurysms and were followed up for an average of 1.82 years, with a recurrence rate of 17.2%. Multivariate analysis revealed that, after controlling for potential confounders, a history of smoking - whether current or former - was associated with a significantly increased risk of aneurysm recurrence. The odds ratios for aneurysm recurrence for

current and former smokers were 2.739 (95% CI 1.127–7.095, $p = 0.0308$) and 2.698 (95% CI 1.078–7.212, $p = 0.0395$), respectively, compared with never smokers.

Conclusions

A positive smoking history is associated with a significantly increased risk of aneurysm recurrence in patients who have undergone endovascular repair of a cerebral aneurysm, compared with the risk in patients who have never smoked

Commentary

Ruvini Abeygunaratne
Consultant Neurosurgeon
Lanka Hospitals PLC, Sri Lanka

A Subarachnoid hemorrhage is a devastating neurosurgical emergency. The commonest cause is trauma but those caused by the rupture of cerebral aneurysms suffer with the worse prognosis. There are two recognized methods of treating ruptured aneurysms, the traditional way of placing a clip at the neck of the aneurysm occluding it, surgically or by placing a coil or several into the aneurysm thereby packing it via an endovascular technique. This is done by the radiologists under image guidance. Many studies have been carried out but there still isn't conclusive evidence as to which technique is better in the long term. What we do know is that there are several risk factors, which increase the rupture rate of aneurysms and the recurrence of aneurysms after treatment. Being female increase the risk as does smoking, being hypertensive, use of drugs such as methamphetamines and cocaine. There is also a known increased risk in families. This study has looked retrospectively at endovascularly treated aneurysms and the affect of smoking pre coiling and post coiling. This confirmed a significantly increased risk of aneurysm recurrence in smokers. This should be taken into consideration when consenting these patients for the procedure and help offered to those patients to stop smoking. Counseling is essential, due to the significant mortality and morbidity associated to rupture of the aneurysm due to recurrence.

The Surgeon Volume-outcome Relationship: Not Yet Ready for Policy

Modrall J G, Minter RM, Minhajuddin A, Eslava-Schmalbach J, Joshi GP, Patel S, Rosero EB
Annals of Surgery: May 2018: Volume 267 :
Issue 5 (p863-867)
doi: 10.1097/SLA.0000000000002334

Objective

Increasing surgeon volume may improve outcomes for index operations. We hypothesized that there may be surrogate operative experiences that yield similar outcomes for surgeons with a low-volume experience with a specific index operation, such as esophagectomy.

Background: The relationship between surgeon volume and outcomes has potential implications for credentialing of surgeons. Restrictions of privileges based on surgeon volume are only reasonable if there is no substitute for direct experience with the index operation. This study was aimed at determining whether there are valid surrogates for direct experience with a sample index operation - open esophagectomy.

Methods

The Nationwide Inpatient Sample (2003–2009) was utilized. Surgeons were stratified into low and high-volume groups based on annual volume of esophagectomy. Surrogate volume was defined as the aggregate annual volume per surgeon of upper gastrointestinal operations including excision of esophageal diverticulum, gastrectomy, gastroduodenectomy, and repair of diaphragmatic hernia.

Results

In all, 26,795 esophagectomies were performed nationwide (2003–2009), with a crude in-hospital mortality rate of 5.2%. In-hospital mortality decreased with increasing volume of esophagectomies performed annually: 7.7% and 3.8% for low and high-volume surgeons, respectively ($P < 0.0001$). Among surgeons with a low-volume esophagectomy experience, increasing volume of surrogate operations improved the outcomes observed for esophagectomy: 9.7%, 7.1%, and 4.3% for low, medium, and high-surrogate-volume surgeons, respectively ($P = 0.016$).

Conclusions

Both operation-specific volume and surrogate volume are significant predictors of in hospital mortality for esophagectomy. Based on these observations, it would be premature to limit hospital privileges based solely on operation-specific surgeon volume criteria.

Commentary

Dakshitha P. Wickramasinghe
Lecturer in Surgery,
Faculty of Medicine,
University of Colombo,
Sri Lanka

The impact of the volume of procedures performed vs surgical outcomes is important in structuring a healthcare system. This article (1) focuses on outcomes after oesophagectomy and found that surgeons who performed over 5

oesophagectomies or 6 surrogate procedures per year had less post-operative mortality compared to surgeons performing fewer cases. Other researchers have identified this extends to length of hospital stay after surgery (2), functional outcomes (2), post-operative complication (3) and 5-year survival (4). Other studies have highlighted that it's the surgeon volume and not the hospital volume that remains the significant predictor of these outcomes (5).

These are important concerns for surgeons managing patients with malignant diseases in Sri Lanka. With the present disparity in the number of surgeons, specialists and resources available, the decision to treat or refer to another centre may be the first crucial decision in managing a patient. This can be further confounded by socio-economic factors of the patients and trends in training surgeons (e.g. selecting a field of "special interest" for general surgeons). The evidence also prejudices against surgeons doing lower volumes at tertiary centres.

Although no Sri Lankan data on volume outcome relationship are available, most surgeons in Sri Lanka perform more than the critical number identified in this study. However, with the increasing number of surgeons and centres, this may soon fall below this value. Therefore, an analysis of local data and evidence based national policies could improve the health care delivery.

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Adoption of Total Neoadjuvant Therapy for Locally Advanced Rectal Cancer

Andrea Cercek et al.

JAMA Oncol. doi:10.1001/jamaoncol.2018.0071

Published online March 22, 2018.

Abstract

Importance

Treatment of locally advanced rectal (LARC) cancer involves chemoradiation, surgery, and chemotherapy. The concept of total neoadjuvant therapy (TNT), in which chemoradiation and chemotherapy are administered prior to surgery, has been developed to optimize delivery of effective systemic therapy aimed at micrometastases.

Objective

To compare the traditional approach of preoperative chemoradiation (chemoRT) followed by postoperative adjuvant chemotherapy with the more recent TNT approach for LARC.

Design, setting and participants

A retrospective cohort analysis using Memorial Sloan Kettering Cancer Center (MSK) records from 2009 to 2015 was carried out. A total of 811 patients who presented with LARC (T3/4 or node-positive) were identified.

Exposures

Of the 811 patients, 320 received chemoRT with planned adjuvant chemotherapy and 308 received TNT (induction fluorouracil- and oxaliplatin- based chemotherapy followed by chemoRT).

Main outcomes and measures

Treatment and outcome data for the 2 cohorts were compared. Dosing and completion of prescribed chemotherapy were assessed on the subset of patients who received all therapy at MSK.

Results

Of the 628 patients overall, 373 (59%) were men and 255 (41%) were women, with a mean (SD) age of 56.7 (12.9) years. Of the 308 patients in the TNT cohort, 181 (49%) were men and 127 (49%) were women. Of the 320 patients in the chemoRT with planned adjuvant chemotherapy cohort, 192 (60%) were men and 128 (40%) were women. Patients in the TNT cohort received greater percentages of the planned oxaliplatin and fluorouracil prescribed dose than those in the chemoRT with planned adjuvant chemotherapy cohort. The complete response (CR) rate, including both pathologic CR (pCR) in those who underwent surgery and sustained clinical CR (cCR) for at least 12 months posttreatment in those who did not undergo surgery, was 36% in the TNT cohort compared with 21% in the chemoRT with planned adjuvant chemotherapy cohort.

Conclusions and relevance

Our findings provide additional support for the National
The Sri Lanka Journal of Surgery 2018; 36(1): 51-54

Comprehensive Cancer Network (NCCN) guidelines that categorize TNT as a viable treatment strategy for rectal cancer. Our data suggest that TNT facilitates delivery of planned systemic therapy. Long-term follow-up will determine if this finding translates into improved survival. In addition, given its high CR rate, TNT may facilitate non-operative treatment strategies aimed at organ preservation.

Commentary

Pramodh Chandrasinghe

Faculty of Medicine

University of Kelaniya

Sri Lanka.

Concept of total neoadjuvant therapy (TNT) that involves a longer chemotherapy regimen following the chemo-radiation (CRT) has caused much debate amongst the scientific community. Argument for it appears to be scientifically sound as it aligns with the theory of cancer being a systemic disease from early stage. As long as the primary tumour does not cause obstruction of the rectum it is sensible to address the micro-metastasis, which is eventually responsible for cancer specific death. Delaying the chemotherapy due to surgery for a non-obstructing tumour gives time for the micro-metastases to consolidate at the new site. An argument against it is that it delays surgery that may cause the tumour to advance locally and metastasize as well. Both arguments are not yet backed by a survival advantage although oncologists tend to increasingly recommend TNT. This study done at the Memorial Sloan-Kettering Cancer center in New York suggests the possibility of total neoadjuvant therapy being superior to CRT plus adjuvant therapy in locally advanced rectal cancer. Their study revealed that those having TNT had 1) better tolerance and completion rates of chemotherapy, 2) higher complete response rate (clinical and pathological) and 3) higher non-operate rates due to complete pathological response. The study further elaborates on observing the same advantage when the difference in time between chemotherapy and surgery in the two groups was adjusted for. It would be interesting to observe the 5 and 10 year survival data from this cohort and pooled data from other centers in the future. The trend may be shifting towards more comprehensive chemotherapy regimens preoperatively for LARC with increase understanding in cancer biology and improved staging with MRI imaging.

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Effect size, confidence interval and statistical significance: a practical guide for biologists

Shinichi Nakagawa, Innes C. Cuthill

<https://doi.org/10.1111/j.1469-185X.2007.00027.x>

Abstract

Null hypothesis significance testing (NHST) is the dominant statistical approach in biology, although it has many, frequently unappreciated, problems. Most importantly, NHST does not provide us with two crucial pieces of information: 1) the magnitude of an effect of interest, and 2) the precision of the estimate of the magnitude of that effect. All biologists should be ultimately interested in biological importance, which may be assessed using the magnitude of an effect, but not its statistical significance. Therefore, we advocate presentation of measures of the magnitude of effects (i.e. effect size statistics) and their confidence intervals (CIs) in all biological journals.

Combined use of an effect size and its CIs enables one to assess the relationships within data more effectively than the use of *p* values, regardless of statistical significance. In addition, routine presentation of effect sizes will encourage researchers to view their results in the context of previous research and facilitate the incorporation of results into future meta-analysis, which has been increasingly used as the standard method of quantitative review in biology. In this article, we extensively discuss two dimensionless (and thus standardised) classes of effect size statistics: *d* statistics (standardised mean difference) and *r* statistics (correlation coefficient), because these can be calculated from almost all study designs and also because their calculations are essential for meta-analysis. However, our focus on these standardised effect size statistics does not mean unstandardised effect size statistics (e.g. mean difference and regression coefficient) are

less important. We provide potential solutions for four main technical problems researchers may encounter when calculating effect size and CIs: (1) when covariates exist, (2) when bias in estimating effect size is possible, (3) when data have non-normal error structure and/or variances, and (4) when data are non-independent. Although interpretations of effect sizes are often difficult, we provide some pointers to help researchers. This paper serves both as a beginner's instruction manual and a stimulus for changing statistical practice for the better in the biological sciences.

Commentary

Dileepa Ediriweera,

Lecturer in Medical Informatics at Faculty of Medicine,
University of Kelaniya,

Sri Lanka.

This article highlights the importance of reporting the effect size in biological research. Hypothesis testing can be performed either with a significance testing or constructing a confidence interval (CI) for an estimate. Significance testing provides a *P* value, which is used to reject or retain the null hypothesis. However, significance testing does not provide information on the magnitude of the effect (i.e. effect size) or the precision of the estimate which is obtained in the study. Statistical significance does not reflect clinical relevance of an outcome a study and presenting the effect size with confidence interval assist researchers to assess clinical relevance and conduct future meta-analysis. Confidence interval of an estimate depends on the sample size and smaller sample sizes results wider confidence intervals and enables researchers to compare results between studies. Therefore, it is advisable to present effect size and their confidence intervals in all biological researchers.