The Journal of
Bone & Joint Surgery

Journal club: 26 October 2011
Chair: Mr. N. Wilson
Organiser: Mr. David Russell, StR 4 West of Scotland Rotation
West of Scotland Orthopaedic Journal Club

Theme: Basic Science

Statistics in Orthopaedic Papers
Petrie A
J Bone Joint Surg [Br] 2006;88-B:1121-36

Reviewer Mr. Vliem Soon, Orthopaedic Registrar, West of Scotland

Fundamental concepts such as study types (observational vs experimental) and variables (categorical vs. numerical) are described. Observational studies can be cross-sectional or longitudinal and the latter can either be prospective (cohort study) or retrospective (case control study). Relative risks and odd ratios are means of quantifying the possible relationships between variables and observed outcomes in observational studies. Case series, randomised controlled trials and blinding are all clearly defined. Evidence based medicine and the hierarchy of evidence levels are also highlighted.

Descriptive statistics covers the presentation of data in relevant tables or charts, and measures such as mean, median, standard deviation and range that help summarise the data.

Inferential statistics is the process of using collected data to test hypotheses in order to reach a conclusion. The statistical test used depends on an understanding of the type of data and outcome in question. Petrie advises the following questions to help choose the appropriate test.

1. Is variable categorical or numerical?
2. How many groups are being compared?
3. Are the groups independent or not?
4. Are the assumptions underlying the proposed test satisfied?

Type I (incorrectly rejecting null hypotheses) and Type II errors (wrongly accepting null hypotheses) can occur during analysis. Power analyses are required when designing a study so that the appropriate sample size is recruited, depending on the significance level, power of the test (chance of rejecting a fall null hypothesis) and the magnitude of treatment effect.

There can be a linear relationship between two variables (*x* – explanatory variable; *y* – dependent variable). A scatter diagram illustrates this relationship and the Pearson correlation coefficient (*r*) is a measure of it. Residuals (difference between observed *y*-value and predicted value from equation) are a way to check that assumptions are met and results valid. The square of the correlation coefficient (r^2) describes the proportion of one variable which can be explained by its linear relationship with the other. Similarly, the Spearman correlation coefficient gives an assessment of association between one or two ordinal variables.

Multiple linear regression is used when there are several explanatory variables (covariates) and a single dependent variable. Adjustments for other covariates are made when producing regression coefficients for each covariate respectively. Logistic regression analysis is used when the dependent variable is binary (e.g. success / failure) and odds ratios are calculated. The Poisson regression analysis is used when length of follow up is variable. The Kaplan-Meier survival analysis is used when investigating the effect of a single variable on survival.

The sensitivity (chance of detecting true positives) and specificity (chance of detecting true negatives) of a diagnostic test provides information on how accurate and useful it is. The Kappa statistic is a useful measure of intra- and inter-observer variability when assessing categorical data. When the data is numerical, the Bland-Altman approach is used.

This paper provides a very good review of statistics aimed at the author of scientific articles in a systematic manner that is relevant to orthopaedic research with the use of good examples and flowcharts. It also highlights the common errors made during statistical analysis.

The anabolic and catabolic responses in bone repair
Little DG, Ramachandran M, Schindler A.
J Bone Joint Surg [Br] 2007; 89-B: 425-33

Reviewer: Mr. Colin Drury, StR 5, West of Scotland Region

Background
Traditionally, failure of fracture union can be described in terms of delayed union, hypertrophic non-union and atrophic non-union. However, these descriptive terms do not specify the various mechanical, biological or pharmacological reasons for failure of complete union. The authors consider the process of bone and fracture repair as consisting of anabolic (bone forming) and catabolic (bone resorbing) responses. Overall union can be, therefore, viewed as a product of these competing inter-related processes.

Summary
Failure of fracture union can be classified as a result of deficient anabolic activity, excess catabolic activity or a net reduction in bone repair due to a combined anabolic and catabolic dysfunction. Evidence exists to suggest anabolic deficiency in fractures with associated soft tissue damage, due to damage to local osteoprogenitor cells. Similarly, the concept of catabolic excess is supported by the increased osteoclast regulation observed in animal models of rigidly fixed fractures.

Existing pharmaceutical therapies can be categorised according to their influence on the underlying anabolic/catabolic responses. Evidence suggests bone morphogenic proteins, such as BMP-2 and OP-1, are local anabolic agents leading to recruitment and proliferation of osteoblast progenitors. Parathyroid hormone is a systemic anabolic agent, when administered in intermittent doses, stimulates osteoblast activity. Nitrogen containing bisphosphonates have an anti-catabolic effect by delaying bone remodeling, thus increasing the overall mineral density and volume of new bone at the fracture site. Animal models have shown these effects may be most pronounced as an adjunctive treatment to distraction osteogenesis of fractures. Other animal studies have shown that the timing of optimal anti-catabolic therapy may be at one to two weeks post injury, when bone formation has commenced. Furthermore, animal studies have shown a synergistic effect with OP-1 and zoledronic acid therapy, which provides a potent anabolic stimulus with limitation of the overall catabolic processes. Co-treatment led to an increase in the volume and mechanical strength of the callus compared with controls and those treated with OP-1 alone.

Conclusions
The anabolic/catabolic model provides an intuitive way of assessing new biological treatments for bone repair. Modulation of the anabolic and catabolic responses can generate profound changes in bone repair with the synergistic effect of anabolic therapies coupled with anti-catabolic therapies providing the optimal response.

Strengths

- Well written
- Clear explanation of new model of bone repair
- Aids understanding of underlying bone physiology
- Provides useful concepts for targeting new therapies
- May be possible to identify patients at risk of delayed union/no-union and target therapy accordingly

Weaknesses

- Limited evidence from animal studies
    - Would in vitro results provide the same clinical benefit?
    - Animal models have short time span
    - Effect of systemic patient factors not considered
- Theoretical model
    - Authors illustrate many models of anabolic/catabolic imbalances but the net effect illustrated is theoretical
- Lack of clinical evidence

An AOA Critical Issue. How to Read the Literature to Change your Practice: An Evidence-Based Medicine Approach
Shurwitz S.R., Tornetta P., Wright J.G.
J Bone Joint Surg [Am] 2006;88-A:1873-1879

Reviewer: Ms. Nadia Claire Sciberras

Evidence-based medicine (EBM) is defined by the authors as being a process that uses truthful clinical information in addition to the practical experience of the surgeon to make medical decisions. Through this paper the authors wanted to acquaint the reader with some of the terminology used, to demonstrate some of the principles of evidence-based medicine and to help orthopaedists to locate the requisite evidence.

The authors start by describing the five stages involved in evidence-based medicine, namely:

1. Formulating answerable questions
2. Gathering evidence
3. Evaluating the evidence
4. Putting evidence into practice
5. Evaluating the results of putting the evidence into practice.

The authors stress the need that orthopaedic surgeons should be more knowledgeable in the use and meaning of statistics and outcome measures as this will enable surgeons to arrive at a more correct conclusion on the basis of the data presented. Consequently, the authors proceed to define some common statistical definitions in a clear way by using examples relevant to orthopaedics. In the same way, they define different types of studies and how at times case series are more suitable than randomised controlled trials as is the case when one is trying to investigate acetabular fracture fixation. However, the authors remind us that it is important that when one critically analyses the data in favour of a particular type of fixation, one should be aware of one's capabilities and limitations prior to introducing the change in one's own practice. It is also important to note that papers with negative findings are as important as those papers that do show significant difference for various reasons. As a start, no difference may exist between two particular methods. Furthermore, most studies in orthopaedics are under-powered thereby failing to reach significant difference.

The authors proceed to discuss the various means available through which we can find the evidence such as (1) peer-reviewed journals that publish outcomes of trials and systematic reviews of trials, (2) medical search engines that gather various publications to give a more complete picture of evidence and (3) presentations and forums. One must be aware that although expert surgeons are content experts they are not necessarily purveyors of best evidence.

Since evidence-based medicine provides the surgeon with the probability of success of a treatment, our practice should change from an opinion-based medicine to evidence-based medicine. As most of the times it is not feasible for the surgeon in clinic to look up the literature when confronted by questions, the authors suggest the use of recognised Practice Guidelines that review the literature and use grades of recommendations to evaluate the overall quality of the evidence. In addition, the authors suggest the use of "hot zones" in clinics that enable easy access to the internet.

The authors therefore conclude that evidence-based medicine has the potential to change the orthopaedic culture and improve the quality of care leading to an improvement in patient outcomes and a decrease in financial burden.

Strengths

- Simplifies what at times is seen as a difficult topic

- Explains the statistical terminology using orthopaedic related examples
- Gives practical examples on how we can use EBM in the clinical setting

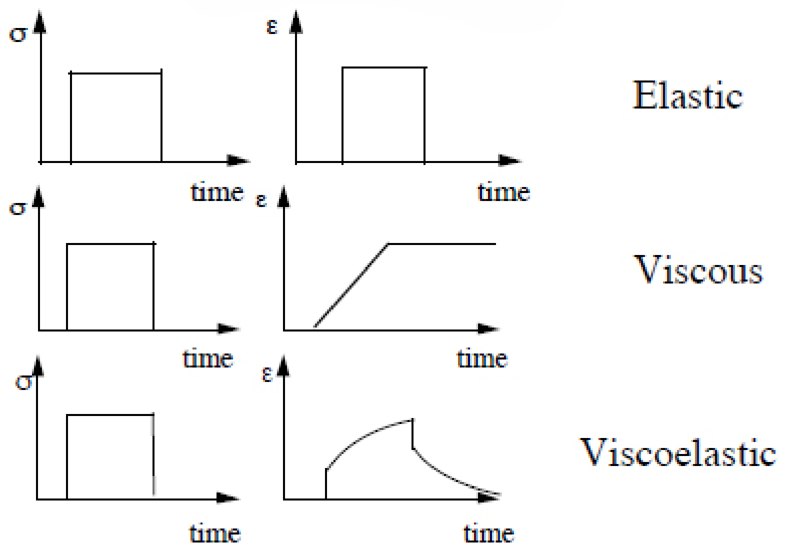
Clinical Relevance

This paper is clinically relevant as it demonstrates the need to change our practice towards one that is evidence-based. It demonstrates the fundamental steps that are involved in evidence-based medicine by using simplified terminology. In addition it also gives us practical ways as to how we can achieve evidence-based medicine in our practice.

Principles of biomechanics and biomaterials in orthopaedic surgery.
Golish SR, Milhalko WM
J Bone Joint Surg [Am] 2011; 93-A: 207-212

Reviewer: Mr. Alistair Stewart Brydone

Article type: Instructional/Tutorial Article
This review intended to cover the "basic aspects of biomaterials relevant to clinical practice including their mechanical properties and uses for implants", and "the clinically relevant aspects, principles, and facts that are germane to many surgical decisions."
Three pages (50%) of the article were dedicated to the explanation of the stress-strain diagram. This basic theoretical model can be applied to any biomaterial to describe its mechanical behaviour. The content and quality of this section were good, the terms were defined clearly an aimed at the appropriate level. Stress, however, is more commonly measured in MPa rather than N/mm^2 and Young's modulus is the modulus of elasticity for tensile loading (rather than strength). The diagram demonstrating visco-elastic behaviour, correctly shows that if an instantaneous stress is applied, the resultant strain will not be linear. Normally however, one would expect an initial large increase in strain, followed by an exponential change, and the opposite would be seen on release of the stress. The diagram below shows examples of elastic, viscous and visco-elastic materials (σ = stress and ε = strain).



Corrosion is an important consideration of metals and this article describes this well and relates the processes to clinical practice.
The paragraph entitled “mechanical properties of common materials in orthopaedics” described only the mechanical properties of metals by reference to the table. It did not include other orthopaedic biomaterials such as ceramics, polymers, glasses and (most importantly) bone. It was stated in the text “the more similar a materials mechanical properties are to bone, the less stress shielding is created”. Unfortunately, when perusing this article in isolation, the reader is not in a position to assess the mechanical merits of the four metals quoted for clinical use.
The metals were described with reference to the American Society for Testing and Materials (ASTM number). It is sometimes more clinically relevant to described biomaterials by both their chemical formula and trade name. *ASTM F-1295* is Protosul® 100 (Ti-6Al-7Nb) and *ASTM F-2063* is Nitinol (Ti-Ni). The behaviour of biomaterials can be altered by using different fabrication methods. Therefore, different biological responses can be achieved using the same (for example) alloy of titanium. It is often preferable to use the trade name of biomaterials as this will potentially define the processes used in manufacture and will give a more specific description of the material.
Article critique

Strengths:

- Concise (only 6 pages)
- Describes stress-strain relationship well (>50% paper)
- Well written and terminology is clear

Weaknesses:

- Limited description of biomaterials other than titanium alloys
- An introduction to implant failure and tribology would have been good

Acknowledgements: Thanks to Professor Elizabeth Tanner from the University of Glasgow School of Engineering for her very helpful advice and for providing the stress-strain diagrams.