

## ORIGINAL COMMUNICATION

## Evidence-Based Anatomy

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Anatomy is a descriptive basic medical science that is no longer considered a research-led discipline. Many publications in clinical anatomy are prevalence studies treating clinically relevant anatomical variations and reporting their frequencies and/or associations with variables such as age, sex, side, laterality, and ancestry. This article discusses the need to make sense of the available literature. A new concept, evidence-based anatomy (EBA), is proposed to find, appraise, and synthesize the results reported in such publications. It consists in applying evidence-based principles to the field of epidemiological anatomy research through evidence synthesis using systematic reviews and meta-analyses to generate weighted pooled results. Pooled frequencies and associations based on large pooled sample size are likely to be more accurate and to reflect true population statistics and associations more closely. A checklist of a typical systematic review in anatomy is suggested and the implications of EBA for practice and future research, along with its scope, are discussed. The EBA approach would have positive implications for the future preservation of anatomy as a keystone basic science, for sound knowledge of anatomical variants, and for the safety of medical practice. *Clin. Anat.* 27:847–852, 2014. © 2014

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## INTRODUCTION

Anatomy is a sequential subject in which knowledge acquired is subsequently elaborated upon. Inadequate knowledge of structure can affect the future understanding of function and dysfunction, and eventually the knowledge and skills concerning therapeutic modalities.

Regarding the current status of anatomical teaching in medical schools, there is worldwide unanimity about the steady decline in the provision of contact hours of this basic science in a crowded undergraduate curriculum (General Medical Council, 2003; Smith, 2005; Tibrewal, 2006; Fitzgerald et al., 2008). Gross anatomy is also perceived by some as a diminished science because it is no longer considered a research-led discipline (Dyer and Thorndike, 2000; McLachlan and Patten, 2006); the majority of “anatomical” published papers in clinical journals are case reports of an anomaly or a variation, cadaveric or radiological prevalence studies, or descriptions of new surgical approaches.

This article introduces the new concept of evidence-based anatomy: the application of evidence-

based principles, mainly evidence synthesis via systematic reviews (SR), to the science of anatomy. Throughout this article, the term “anatomy” will be used to refer mainly, but not exclusively, to the field of clinical anatomy.

## ANATOMY AND ANATOMICAL VARIATIONS

The history of human anatomical variations is the history of anatomy itself (Sañudo et al., 2003), and I would add that the future of anatomy depends on future methods for studying anatomical variations.

Vesalius, after Galen, is credited for being the father of modern anatomy owing to his work *De*

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*Humani Corporis Fabrica* (Vesalius, 1542 [cited in Garrison and Hast, 2003]), which contains numerous references to anatomical variations (Straus and Temkin, 1943; Hast and Garrison, 2000). In fact, locating the boundaries of normality is not easy, and it took several decades of observations until a compendium of human anatomical variations was published (Bergman et al., 1988, 2002). In 2006, the editorial board of the journal *Clinical Anatomy* took a step forward in indexing and publishing rare anatomical variations (Carmichael, 2006). However, as is commonly known, the anatomy of organisms is not the same within each species, and this applies *inter alia* to humans. Therefore, the scope of anatomical variations cannot be limited to variants or anomalies; it also encompasses “normal” variation among individuals. This is why anatomical variations have to be considered an integral part of anatomy teaching; knowledge of common variants reflects the ability to recognize the diverse clinical reality of anatomy.

Anatomical variations can be grossly divided in three categories: morphometric (size and shape), consistency (presence, absence, or multiple), and spatial (proximal/distal or right/left bifurcation, arterial supply, etc.). Many such anatomical variations are of clinical relevance. For instance, knee implant manufacturers design total knee implants on the basis not only of size differences but also of sex and ethnicity. The multiple anatomical variants associated with median nerve anatomy and the causes of its compression afford another example of vulnerability to injury during surgical operations (Beris et al., 2008; Khan and Giddins, 2010; Brüser, 2011; Budhiraja et al., 2012). Knowledge of the anatomical variations of the cystic artery has been considered a precondition for performing safe laparoscopic cholecystectomy (Ding et al., 2007). Furthermore, suboptimal anatomical knowledge has been linked to an increase in some types of medico-legal claims, many of which have been related to “damage to underlying structures” and viewed as a threat to patient safety (Ellis, 2002; Regenbogen et al., 2007). Cahill and Leonard (1999) reported that 10% of clinical malpractice is due to ignorance of anatomical variations. Many believe that malpractice due to suboptimal knowledge of anatomy is underreported; not every “anatomical” complication is documented (Kernt and Neu, 2011), and even if it is documented, it is not necessarily reported or published (Leppäniemi and Clavien, 2013; Slankamenac et al., 2013). Moreover, in clinical practice, some surgical “mistakes” do not lead to clinical complications, such as an iatrogenic injury to the radial artery via a distal “Henry” approach while placing an anterior plate for distal radius fractures; nonetheless, they indicate a substandard knowledge of anatomy.

## EVIDENCE-BASED PRINCIPLES

Evidence-based principles (EBP) were first used in medicine under the label “evidence-based medicine” (EBM), which is defined as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients” (Sack-

ett et al., 1996). Since its inception, the evidence-based movement has gained huge popularity and taken a major place in almost all aspects of medicine, and subsequently in other fields such as allied health therapies, educational and sociological research, business management, and conservation biology (Ader et al., 2008).

Commonly, the concept of EBM is based on stratification of five levels of evidence, known as the evidence hierarchy, ranging from meta-analyses (MA) with homogeneous results of high-quality Level I randomized controlled trials (RCT) to expert opinion—Level V (Evidence-Based Medicine Working Group, 1992). Study designs such as quasi-randomization, prospective and retrospective comparative, case-control, and case series studies are located between these extremes. Systematic reviews (SR) of high-quality RCTs form the top of the evidence hierarchy, particularly for interventional assessment (Sackett et al., 1996), and those of “lesser” study designs are considered to have lower levels of evidence. A SR is defined as a review focusing on a narrow research question that identifies, appraises, and selects the evidence available in the literature to obtain a high-quality evidence synthesis. SRs have increasingly replaced traditional narrative reviews and expert views as ways of summarizing evidence. The purpose is to sum up the best available research on a specific question using transparent and repeatable predefined procedures to find, evaluate, and synthesize the results of relevant research papers ([www.campbellcollaboration.org](http://www.campbellcollaboration.org), accessed on Dec. 14, 2013). Often, but not always, a statistical method named meta-analysis is used to combine the results of eligible studies in order to generate a pooled estimate reflecting the overall weighted average, in relation to sample size, of the effect estimates from the included studies ([www.cochrane.org/training/cochrane-handbook](http://www.cochrane.org/training/cochrane-handbook), accessed on Dec. 14, 2013).

## EVIDENCE-BASED ANATOMY

Historically, the work of Vesalius was not limited to a simple documentation of the variations he encountered or studied; he used “subjective statistics” in an attempt to estimate their occurrence in humans. Straus and Temkin (1943) [cited in Sañudo et al. (2003)] noticed an abundance of expressions in Vesalius’ book that can be translated into “always,” “usually,” “frequently,” “more frequently,” “most frequently,” “sometimes,” “not always,” “rarely,” “relatively rarely,” “much more rarely,” and “very rarely.” The use of basic descriptive statistics in anatomical papers can be traced to the end of the 18th century when some clinicians and anatomists reported frequencies and subgroup rates of anatomical conditions (Pfitzner, 1892; Fawcett, 1896; Thilenius, 1896). Since then, the full range of descriptive and inferential statistics has frequently been used in anatomical publications. On the other hand, those publications are mainly transversal studies, also known as cross-sectional or prevalence studies, where frequency data are collected at a single point in time. Such a study

design is of interest for epidemiological research in anatomy; apart from studies of the effects of surgical approaches on patient outcomes, RCTs do not have a place in clinical anatomy and case-control studies are exceptional.

"Evidence-based anatomy" might appear to be a weird association of terms. It is true that anatomy is a "dry" descriptive basic science; however, morphometric and epidemiological studies of anatomical structures include: (a) measurements with their descriptive statistics used to define the "normal" range of morphometric variation, (b) frequencies to assess inconstant structures, and (c) basic inferential statistics to look for associations with variables or differences among groups. Data derived from observational anatomical studies are mainly means with standard deviations, prevalence, and odds ratios. Such data collected from studies meeting predefined inclusion criteria will be subject to meta-analysis to yield weighted pooled estimates. It is believed that results drawn from a large pooled sample are likely to be more accurate and to reflect true population statistics and associations more closely. Hence, meta-analytical results of anatomical prevalence studies are considered the mainstay of EBA.

## THE APPLICATIONS OF EBA

Evidence-based principles in anatomy could be applied to enhance the design of observational studies and to perform systematic reviews. In fact, while conducting our "anatomical" SRs, we were surprised by the number of studies describing the prevalence of a condition with poor reporting of: (a) subjects' baseline characteristics such as age, sex, or side of the condition, (b) study characteristics such as retrospective or prospective design, (c) the diagnostic tools such as the radiographic views used to diagnose the condition, and/or (d) outcomes of interest such as side-based or sex-based frequencies. Obviously, there is room for improvement, and editors should encourage investigators to report such information whenever possible. An EBA approach would incite researchers to conduct prospective studies based on premeditated and well-thought-out designs.

However, I believe that efforts should not be limited to reporting new variations or their occurrence in a specific population. It is time for the science of anatomy to join the evidence-based movement. There is a need to make sense of what has been published and this could be achieved through evidence syntheses such as SRs and MA. The literature is now rich in prevalence studies and it is worth using meta-analytical techniques to obtain more accurate frequency estimates in relation to anatomical conditions. The first published SRs and MA conducted in our Center for Evidence-Based Sports and Orthopedic Research (CEBSOR) yielded overall and subgroup prevalence values, on muscle agenesis such as the Palmaris Longus, and occurrence of bone structures such as the os acromiale and the sesamoids in the hands (Yammine, 2013, 2014a; 2014b). Since the pooled sample size in each review was large, associations with side, sex,

laterality, and ancestry were also calculated. More, data analysis yielded quantitative evidence favoring one etiological hypothesis over another; for instance, the genetic rather than the functional basis of all our studied conditions was supported. Besides the aforementioned papers, and as far as I know, the application of evidence-based principles to anatomy has not been described or used before in the literature, at least not systematically.

I need to emphasize on the value accorded to the pooled results obtained via MA; those results are neither dogmatic nor do they indicate the true population prevalence of a studied condition. A pooled result is a best estimate; conclusions drawn from MA results are interpretations of the best evidence available when the SR was conducted.

## HOW TO CONDUCT A SYSTEMATIC REVIEW IN ANATOMY

On the basis of our recent experience, we will describe the steps needed to conduct a typical SR, along with some tips relevant to epidemiological research applied to anatomy, the most frequently used types of measuring effects, the basic principles of meta-analysis, the limitations and bias encountered, and the conclusions that can be drawn from such research design.

Many checklists have been proposed to assist authors conducting SRs. Some are focused on interventional studies such as the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009); others are dedicated to observational studies, such as the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement (von Elm et al., 2007) and the MOOSE (Meta-analysis of Observational Studies in Epidemiology) statement (Stroup et al., 2000). Most studies relevant to epidemiological research in anatomy are observational, mainly cross-sectional, and are used to determine the prevalence of anatomical variations. A checklist of a typical SR in anatomy has been established after reviewing all three statements. The "Checklist for Anatomical Reviews and Meta-Analyses" (CARMA) is a simplified version of the above statements in which the given details of each item are relevant to the specific field of anatomy (Table 1). Updating published SRs in anatomy (e.g., every 2 years) would offer the possibility of increasing the pooled sample size, yielding potentially better estimates.

## USEFUL TIPS FOR SRs IN ANATOMY

Initially, it can be very helpful for anatomists and clinicians conducting MA to consult a medical statistician; afterward, statistical competence can be relatively easily achieved. However, evidence synthesis via SRs in anatomy has some specificity, and a few tips could help for the following three steps:

**TABLE 1. Checklist for Anatomical Reviews and Meta-Analysis (CARMA)**

Title	The title should include the main objective of the study, usually the primary outcome such as the prevalence of an anatomical condition, and, the study design, which in our case should be SR or SR with meta-analysis.
Abstract	The abstract should include the objective of the review, the primary and secondary outcomes, the total number of included studies, the overall and subgroup pooled prevalence results with their confidence of intervals, and the results of any association or correlation, when applicable.
Methods	<p>The objective (s) should be clear while providing an explicit statement of the question(s) being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). In the field of anatomy, the outcome for a SR is usually a pooled prevalence from cross-sectional studies in which the subjects are individuals, cadavers and/or skeletons. Comparisons could be between different age, sex or ancestry groups, or between diagnostic-based prevalence values (e.g.: . cadaveric vs. radiological).</p> <p>Description of eligibility criteria such as study characteristics (PICOS) and report characteristics (e.g., years considered, language). However, in anatomical epidemiology, the sample size and the number or rate of the condition should be available for a study to be included. If possible, there should be no restriction to language or years; the larger is the pooled sample size, the greater is the accuracy of the results. When possible, reasons for exclusion should also be reported.</p> <p>Description of all information sources such as databases with dates of coverage and contact with study authors in order to identify additional studies. However, electronic archives, grey literature and hand-searching could potentially be very useful for searching of related articles and in particular old anatomical publications. Such resources should also be reported.</p> <p>Description of the search strategy and reporting the full electronic search strategy for at least one database, including any limits used. Therefore, the strategy could be repeated by anyone.</p> <p>Description of the study selection process; : (a) identification of studies through database searching and other resources; (b) screened abstracts and number of duplicates removed and records excluded; (c) full-text articles excluded and full-text articles assessed; (d) number of included studies.</p> <p>The process of data collection; : description of methods of data extraction from reports and any processes for obtaining and confirming data from studies' authors.</p> <p>Risk of bias; : mainly due to underreporting of study and subjects' characteristics.</p> <p>Description of summary measures; : statement of the principal summary measures. In anatomical epidemiological research, pooled prevalence and pooled odds ratio are the main summary measures while correlation tests are rarely used. Chi-squares and proportion difference tests are also used to look for associations with other variables or to search for significant rate differences between population or subgroup samples.</p> <p>Synthesis of results; : description of methods of handling data and combining results of studies. Measures of inconsistency, such as the <math>I^2</math> statistic, should be reported for each meta-analysis. Generally, an <math>I^2</math> value &gt; 50% is considered to suggest statistical heterogeneity, prompting a random effects modeling estimate. Otherwise, the fixed effects estimate is used.</p> <p>Additional analyses; : description of methods of additional analyses such as sensitivity analyses, mainly by analyzing the large -sampled studies, or subgroup analyses by analyzing the prevalence of the "condition" in specific population groups such as those based on sex or ancestry.</p>
Results	<p>Results of the study selection; : (a) numbers of abstracts screened, (b) studies assessed for eligibility, and (c) studies included in the review, with reasons for exclusions at each stage. A flowchart could be of help if such information is not mentioned in the text.</p> <p>Results of study characteristics are best shown in table formats instead of the traditional presentation of the characteristics of each study for which data were extracted. Usually such tables include the studied population (ancestry), the type of the study (radiological, cadaveric or skeletal), the median age or the age range of the subjects, the total sample size, the sample size for each side, and the sex-based sample size, when possible.</p> <p>Results of individual studies should be reported preferably in table format for main outcomes such as the overall prevalence and study the type-, side-, sex-, laterality-, and ancestry-based frequencies for each study.</p> <p>Synthesis of results; : reporting the pooled result of each meta-analysis done, including confidence intervals and measures of inconsistency.</p> <p>Results of sensitivity or subgroup analyses are reported in the same way.</p>
Discussion	<p>Summary of the main findings including the strength of evidence for each main outcome.</p> <p>Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).</p> <p>Conclusions; : provide a general interpretation of the results in the context of other evidence, and implications for future research.</p>

1. On the sources of information  
Besides the usual search databases and journal hand-searching, two internet-based archives were of interest in locating full-text manuscripts of old articles; the archives of the National Library of Medicine (<https://archive.org/details/usnationallibraryofmedicine>), and Gallica, the numerical library of the National Library of France (<http://www.bnf.fr/fr/acc/x.accueil.html>). On the other hand, contacting the corresponding authors of relevant publications has helped in retrieving unreported data.
2. On the terms used in electronic search strategy  
Our experience demonstrated that broad terms could locate more relevant articles than restricted terms. For instance, while preparing the SR on os acromiale, adding "scapula" to the search term "os acromiale" yielded a further three relevant articles reporting the prevalence of os acromiale.
3. On the search engines  
Some relevant references were located only by Google Scholar, particularly in the case of old textbooks or non-English published articles or books. When manuscripts could not be located on internet, their results could sometimes be found in library or digital textbooks with enough details to justify inclusion in the review.

## THE POTENTIAL OF EVIDENCE-BASED ANATOMY

### Implications for Practice

In this era of quality healthcare and the continuous search for medical excellence, a sound knowledge of anatomical structures and their variations is primary for the outcome of the patients we treat. Using the EBA approach will incite medical teachers to emphasize clinically relevant variants both to medical students and to residents, particularly in surgical specialties and diagnostic/interventional imaging. Furthermore, many variations are associated with variables such as age, sex, and especially ancestry. The ability to estimate the incidence of a variant in different population groups will, therefore, be highly relevant to clinicians worldwide. On the other hand, any compendium of anatomical variations will benefit from EBA; it will include not only descriptive observations but also overall and subgroup prevalence values.

### Implications for Research

We need to reaffirm that SRs of high quality depend on the availability of high-quality prevalence studies. Writing protocols before conducting a prospective study reduces the risk of missing relevant data and their potential for future analysis.

To investigators, more accurate prevalence results yielded by MA will offer valuable data for comparison in future epidemiological research. Such results are also expected to be used widely in reference text-

books and where previous frequencies or associations can be confirmed or refuted by the overall and subgroup pooled results. In fact, rates given in papers and books are frequently repeated although some are based only on expert reviews. Furthermore, evidence synthesis can also contribute to evaluating etiological hypotheses such as genetic, functional, or environmental.

Currently, we are exploring potential surgical outcomes that can be related more or less directly to specific surgical approaches. We expect that SRs in surgical anatomy will have the same rigorous checklist as any "interventional" SR such as those of the Cochrane Collaboration (Higgins and Green, 2011), particularly in terms of bias risk and assessment.

### The Future Scope of EBA

The scope of EBA has the potential to embrace almost all branches in anatomy: gross, microscopic, surface, surgical, and developmental. EBA can be used in osteo-archeology as well; for instance, the SR on the prevalence of os acromiale included skeletal studies and yielded a skeletal prevalence along with the radiological and cadaveric results. Additionally, there will be new opportunities for anatomists to invest in transdisciplinary research over a range of areas such as molecular biology, functional anatomy, physical anthropology, biological anthropology, forensic anthropology, pathology, kinesiology, biomechanics, and biodistance. More pathways of cooperation between anatomists and clinicians are expected to be forged, too.

To conclude, I hope that EBA, by gaining acceptance first among anatomists and clinicians, will revive research interest in the discipline of anatomy by injecting new blood into this basic science through the conduction of systematic reviews and will generate a network for transdisciplinary research. My hope for the near future is that anatomical journals will arrange for an evidence-based review section to help in promoting and fostering the development of EBA. An optimistic prediction can be fairly stated: MA of prevalence studies will constitute a major breakthrough in epidemiological anatomy research. Collaboration between anatomists/clinicians of different backgrounds would be the ideal framework in which to achieve such a goal.

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