A review of the importance of research in Anatomy, an evidence-based science

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SUMMARY

Considered an absolute unchanging truth, and not research-led, human anatomy has been subject to a steady decline in course hours and funding. However, this is a misconstruction, as anatomy plays an important role in the clinical and surgical field, with the need of evidence-based data, more so now than ever. Research in anatomy not only establishes an evolutionary and functional database with variability between populations, sex, and age, but develops the tools needed for patient safety, development of prostheses, technology and surgical materials, improves interpretation of imaging studies, and provides evidence of clinical and anatomical implications. Evidence-based education is an exponentially growing field in anatomical sciences, providing the best evidence for technological and pedagogical strategies integrated in the classroom and laboratory. The gold-standard cadaveric dissections are currently only one of the wide range of educational resources available, with imaging studies and clinical scenarios playing an important role. Anatomy research needs to be continued, evolving with the generations the availability of new resources and the demands of the field. This review breaks down the available data, recommendations, and guidelines, as well as the importance behind the continuing research in anatomical sciences.

Key words: Human anatomy – Anatomical variants – Anatomical sciences – Anatomy education – Evidence-based anatomy – Imaging

INTRODUCTION

Human anatomy as a discipline has historically been the study of the structure and form of the body, as well as the relationships between the different regions. It has been in constant transformation since ancient Mesopotamia and the Greek era, with documents such as the *Corpus Hippocraticum* associated with medical education, Hippocrates "Father of Medicine," and the first evidence of anatomical research and documentation (Edelstein, 1939; López Férez, 1986; Persaud et al., 2014). New dissection techniques were developed, on which Aristotle based human anatomy by comparison with animal anatomy to establish the fundamentals of clinical medicine (Blits, 1999; Crivellato and

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Ribatti, 2007). Galen's anatomy also used animal dissection to base the theory of humoralism, as human dissection was strictly prohibited in this era, limiting the evolution of this science.

It was during the Renaissance era when research influenced the views of modern anatomy in medicine (O'Rahilly, 1997; Cosans, 2015). Leonardo da Vinci contributed with his detailed anatomical drawings based on observation. Corpses were incorporated into anatomical studies, leading to a more systematized study of the human anatomy, and an understanding of the development, structure, and functioning of the body (García Barrios et al., 1999; Álvarez Guisbert and Ro, 2007). the attempt to compensate for lacunae in knowledge was what led Andreas Vesalius to the publication of his work *De humanis corporis fabrica*. His conclusions would set the guidelines for a clear comprehension of anatomy (Malomo et al., 2006; Romero Reveron, 2007), and the beginning of a surgical revolution (Mottershead, 1980; Toledo-Pereyra, 2008; Markatos et al., 2020). However, anatomical knowledge was limited by the scarcity of dissections that reveals absolute truths to the science.

An era of cadaveric anatomy provided a more precise tool for teaching. However, learning was limited by a small sample of bodies, without consideration of the individuals' characteristics, race, diseases, or causes of death. There was a lack of variability and a belief in absolute truths that were later proved erroneous. Preservation techniques also limited the time and availability of specimens, in which structures may change in different aspects. This constrained anatomical research to only descriptive, sometimes comparative studies.

With time and the progression of technology and preservation techniques, the use of cadavers was simplified. Embalming techniques changed from alcohol immersion to the intra-arterial use of chemicals with antimicrobial properties which allowed the conservation of histological appearance, providing anatomists with a wider usability and time frame of usage (Brenner, 2014). The Thiel technique even allows for the preservation of natural colors, without the release of harmful volatile substances. Plastination, based on curable polymers, allows the dry, odorless, durable, non-toxic preservation of specimens stored at room temperature, although the technique requires expensive and specialized infrastructure (Mahajan et al., 2016). Regardless of the technique, anatomists seek to preserve the tissue for longer periods, conserving natural characteristics such as color, tissue softness, and joint mobility. This provided the modernization of gross anatomy research (Brenner, 2014; Balta et al., 2015).

With the scientific evolution of anatomical studies, the teaching of gross anatomy continued as a traditional and methodical science, as was the case for several centuries. With the use of bodies, several anatomists continued to contribute to anatomical knowledge. During the last two decades of the 20^{th} century, the discipline began an important transformation with the incorporation of clinical anatomy and advances in teaching (Higgs, 1992; Elizondo-Omaña and López, 2008; Elizondo-Omaña et al., 2010; Estai and Bunt, 2016). Slowly, problem-based learning and computer-based learning were implemented, with research showing a clear benefit towards the understanding and application of this discipline. Students' interest peaked with the study of clinical cases and the use of digital tools to learn anatomy, complemented with dissections (Walsh and Bohn, 1990; Levine et al., 1999; Older, 2004; Yiou and Goodenough, 2006; Papa and Vaccarezza, 2013). This allowed for the modernization of research, education, and the teaching of anatomy (Drake et al., 2009; Mitchell and Batty, 2009; Sugand et al., 2010; Khalil et al., 2018).

CURRENT PERSPECTIVE

Modern medicine has been transitioning into an evidence-based practice. Gross anatomy, seen as a discipline not research-led, has been subject to a steady decline in the curricula as a stand-alone subject (Yammine, 2014b; McBride and Drake, 2018). Gross human anatomy cannot be left behind. Vertical integration of anatomy has been implemented in many universities, providing assessment strategies to assure that anatomical knowledge and education be kept to the needed standard (Bregman et al., 2011). Senior students and more mature medical residents who have developed broader clinical reasoning can integrate anatomical knowledge (Rajan et al., 2016; Morgan et al., 2017; Quiroga-Garza et al., 2020). Anatomy research must be maintained and furthered purposefully.

Research in anatomy has been developed with the objective not only of establishing the prevalence of variability between different populations, sex, and age, but also of understanding the clinical implications it may have. A detailed study of anatomy helps healthcare providers increase patient safety during surgical procedures, aids in the development of prostheses, technology and surgical materials, improves the interpretation of imaging studies, and provides evidence for these. This is not only through the use of human bodies, but also imaging studies and the use of trans-operative surgical videos. This is what must be called an evidence-based anatomy (EBA) (Yammine, 2014a).

EVIDENCE-BASED ANATOMY

The study of anatomy is relevant to modern medicine, creating a high value in patient safety during surgical procedures (Clifton et al., 2020; Dee et al., 2021). Previous studies have demonstrated that an important percentage of *mala praxis* lawsuits are due to surgical errors attributed to "ignorance about anatomical variations" (10%) (Cahill and Leonard, 1999) and "abnormal or difficult anatomy" (13%) (Rogers et al., 2006).

The Evidence-Based Medicine (EBM) concept was first described in 1992 (Guyatt et al., 1992). It proposed a shift from a pathophysiological comprehension, non-systematized, intuition-based clinical practice to an EBM that requires efficient literature searching and the application of guidelines and recommendations based on the evaluation of the best available evidence (Guyatt et al., 1992; Sackett et al., 1996; Phillips, 2014). Evidence is hierarchically classified from the highest impact (Level 1, i.e., systematic reviews of randomized controlled trials) to the lowest (Level 5, i.e., expert opinions) (Uman, 2011; Phillips, 2014; Henry et al., 2017).

Most anatomical studies in the literature are cross-sectional or prevalence-based with epidemiological ends (Yammine, 2014a). These include anatomical structure measurements with a range of "normality" and its statistical description, inconstant structure frequencies, and inferential basic statistics looking for associations between variables or groups (sex, age, ethnicity).

As it is difficult to perform randomized controlled trials for anatomical studies, meta-analytical results of anatomical studies are considered the base of the EBA. Systematized guidelines for the realization of anatomical systematic reviews have been published (Yammine, 2014a; Henry et al., 2016). This has aided in understanding anatomical variations, which may be due to the differences in population, ethnicity, age, sex, medical history, as well as methodological discrepancies (Rodríguez-Niedenführ et al., 2001; Bergman's Comprehensive Encyclopedia of Human Anatomic Variation, 2016; Abou-Foul and Borumandi, 2016; Ling and Smoll, 2016; Martínez-González et al., 2017; Popieluszko et al., 2018; Santos et al., 2018; Hernandez-Trejo et al., 2020; Muñoz-Leija et al., 2020) For these reasons, AQUA (Anatomical Quality Assessment) guidelines were published as recommendations for researchers to ensure a higher quality of anatomical studies as well as publications (Henry et al., 2016; Henry et al., 2017; Henry, Skinningsrud, et al., 2018; Henry, Vikse, et al., 2018).

RESEARCH IN ANATOMY

Research in anatomy has shifted during the last couple of decades. This is most evident in anatomy journals and publications. Although basic gross anatomy regarding structure, function, development, and evolution is still widely published, a much larger field has opened with a refocus of traditional journals, and the emergence of new journals to publish anatomical research oriented towards the clinical and surgical application, and the advances in the educational field, which has exponentially grown.

Medical education has been constantly changing with a direct impact on modern anatomy teaching. Contemporarily, more anatomy courses are being part of an integrated curriculum in medical schools. Course hours have had a downward trend in the last two decades, due to curricular approaches, class size, and other parameters. However, this trend seems to be stabilizing (Drake, 2014; McBride and Drake, 2018; Salinas-Alvarez et al., 2020). It has evolved from the days of long and continuous lectures to the promotion of active learning, where people might benefit more from different learning styles (visual, auditory, kinesthetic, others) (Carmichael and Pawlina, 2000; Gregory et al., 2009; Andrew Jay et al., 2013; Morton and Colbert-Getz, 2017). Additionally, integration with clinical medicine throughout the course gives students a reason to learn (Lachman and Pawlina, 2006; Drake, 2014; Drake et al., 2014). Through these activities, anatomical education aims to generate in the student acquisition of anatomical knowledge and the development of clinical reasoning skills (Elizondo-Omaña and López, 2008; Elizondo-Omaña et al., 2010; Quiroga-Garza et al., 2020; Gonzalez-Navarro et al., 2021).

Evidence-based education is also guiding the integration of curricula and the approach to teaching anatomy. Educational journals are on the rise, with an increased number of submissions, publications, and citing. Educational studies need to follow recommendations of competency-based objectives to improve the quality of reports, avoiding the over-use of technology (Ganguly, 2010; Cohen et al., 2015; Estai and Bunt, 2016; Clunie et al., 2018; Krebs et al., 2021). Systematic reviews and meta-analyses are providing the best evidence for the implementation of technological and pedagogical strategies integrated into anatomy education (Bergman et al., 2008; Campos et al.,, Sugand and Mirza, 2013; Akçayır and Akçayır, 2017; Li et al., 2017; Clunie et al., 2018; Langlois et al., 2020). However, these must be evaluated and adapted to each environment and individual circumstance in each school and university.

The integration of classroom knowledge and laboratory activities is an important competence. Traditionally, dissection has been the pillar of anatomy, developing professional, bioethical, and psycho-emotional skills in students (Elizondo-Omaña et al., 2005; Ghosh, 2017; Quiroga-Garza et al., 2017). However, obtaining human tissue may be a challenge for several reasons including financial, ethical, legal, and cultural (AbouHashem et al., 2015; Quiroga-Garza et al., 2017; Ciliberti et al., 2018; Habicht et al., 2018; Hasselblatt et al., 2018; McBride and Drake, 2018; Champney et al., 2019; Kostorrizos et al., 2019; Zhang et al., 2020). Cadaver use is decreasing, with alternatives for learning gross anatomy on the rise (McBride and Drake, 2018; McMenamin et al., 2018). A variety of technological educational resources have emerged in recent years to solve these obstacles, with a wide range of peer-reviewed articles discussing their effectiveness (Vázquez et al., 2007; Estai and Bunt, 2016; Zargaran et al., 2020; Krebs et al., 2021).

Imaging has become an increasingly important component in the teaching of anatomy, enhancing the quality and efficiency of learning (Pawlina and Drake, 2015; Grignon et al., 2016; Royer, 2016; Patel et al., 2017). Clinical cases ensured engagement between anatomical knowledge and clinical scenarios, promoting clinical reasoning to encourage learning outside the classroom settings and ultimately improving the decision-making skills (Elizondo-Omaña et al., 2010, 2020; Perumal et al., 2016; Dinesh Kumar et al., 2020; M. Muñoz-Leija et al., 2020; Salinas-Alvarez et al., 2020). Three-dimensional (3D) printing includes an accurate duplication of anatomical structures with both visual and haptic value, and financial alleviation (AbouHashem et al., 2015; Vaccarezza and Papa, 2015). Students can actively interact with the models, creating an integration of kinesthetic and visual learning, highly valuable with complicated anatomical structures (Erolin, 2019). More recently, augmented- and virtual-reality technologies allow students to manipulate a virtual 3D model of an anatomical structure and navigate around them. Interactive hologram teaching technology is currently being developed and experimented (Kuehn, 2018; Darras et al., 2019; Pennefather and Krebs, 2019).

All these tools have aided in the purpose of anatomical studying and its implications in clinical scenarios. However, for a student to integrate this knowledge, the transfer must be vertical. Many anatomy courses are now spread throughout the curricula, providing senior students with an anatomical review in each clinical rotation. (Bregman et al., 2011; Rajan et al., 2016; Morgan et al., 2017). Constant exposure helps students recall the anatomical knowledge needed, to improve their clinical thinking and reasoning, significantly improving their assessment and understanding (Murphy et al., 2014; Osborn et al., 2014).

THE IMPACT OF IMAGING IN ANATOMICAL RESEARCH AND EDUCATION

The change in understanding gross human anatomy due to imaging techniques cannot be overestimated, as their nature allows users to visualize it in the living (Ganguly, 2010). X-rays, ultrasound, computerized tomography, magnetic resonance imaging, and digital subtraction angiography, have advanced the quality and precision of anatomical research. It broadens the options of protocol design and methods, facilitates a larger sample size, and enhances the confidence interval. The imaging software provides millimetric precision to measurements in an objective, reliable, and reproducible manner. It facilitates access to deep structures without the necessity of laborious and lengthy dissections that could alter its structural integrity. Most hospitals count with imaging databases, which upon approval of the Research and Ethics Committees, are of easy access, making them an attractive and effective method for anatomy researchers (Tregaskiss et al., 2007; Elizondo-Omaña and López, 2008; Elizondo-Omaña et al., 2010; Grignon, Oldrini and Walter, 2016; Kobatake and Masutani, 2017).

Imaging also revolutionized anatomy education. It allows an easier and three-dimensional understanding of anatomy for students. Typical anatomy can be compared to pathological findings. Ultrasounds can be used to view real-time anatomy. It has aided in the development of anatomical virtual and augmented reality. All these, without the need for expensive dissection laboratories (Machado et al., 2013; Phillips et al., 2013; Pawlina and Drake, 2015; Estai and Bunt, 2016; Moro et al., 2017).

ANATOMICAL VARIANTS AND THEIR IMPORTANCE IN CLINICAL SCENARIOS

Normalis means "by the rule or pattern". "Normal anatomy" refers to the ideal, typical, mean, natural, or most frequent (Moore, 1989). However, in the study of anatomy, normality involves a range of normal variations. Abnormal variables can be major or minor, derived from aberrant development processes during the formation of a structure by genetic, chromosomal, or environmental influences (Sañudo et al.,, 2003; Bergman's Comprehensive Encyclopedia of Human Anatomic Variation, 2016).

Galen and Vesalius noted variations in their respective investigations. Expressions like "always", "usually", "frequently", "more frequently", "sometimes", "not always", "rarely" and, "very rarely", can be found in their works (Straus et al., 1943). Centuries and several dissections were the basis to establish the concepts of normality, abnormality, and variations of the human body, thanks to the reported knowledge in works of many biologists, clinicians, and anatomists since the 19th century until today (Sañudo et al., 2003; Bergman's Comprehensive Encyclopedia of Human Anatomic Variation, 2016).

Despite numerous studies carried out over the years, the anatomy of structures continues to be researched. Significant variability of the shaping of systems and regions has been drawing attention for years and inspires targeted research projects. The future of anatomical research depends greatly on the imaging methods for anatomical variabilities. These can be gathered into three categories: morphometrical, consistency, and spatial (Yammine, 2014a).

Anatomical variability is valuable not only from the anatomical point of view but also in the clinical aspect, due to their implications (Cahill and Leonard, 1999; Rogers et al., 2006). For example, the atypical variations of the anterior cerebral artery and the communicant anterior artery increase the risk of stroke (Jiménez-Sosa et al., 2017). To understand the pathophysiology of compartment syndrome of the foot and develop viable treatment options, a clear knowledge of the foot compartments is needed (Vazquez-Zorrilla et al., 2020). At a diagnostic level for perineural metastasis, it is useful to keep in mind the variations in the asymmetry of the skull base canals (Barrera-Flores et al., 2017). At a surgical level, to avoid complications in a paranasal sinuses surgery, ethmoidal roof variations and differences between gender must be considered (Muñoz-Leija et al., 2018). At a treatment level, the location (origin, pattern, branches) of the bronchial arteries is vital for their embolization to control massive hemoptysis (Esparza-Hernández et al., 2017), or of the external carotid artery when performing a neck procedure (Herrera-Núñez et al., 2020). Justification of procedures, such as the measurement of the pelvic and birth canal to determine cephalopelvic disproportion were an indication for a cesarean section (Vázquez-Barragán et al., 2016). The physiological changes of the recto-vaginal septum due to gynecological history influence the risk of fistulae formation (Rodríguez-Abarca et al., 2020). The influence of a higher hippocampal volume to achieve remission in depression (Zarate-Garza et al., 2021). Facilitating a procedure such as right internal jugular vein catheterization by increasing its size with a degree of head-down tilt position (Garcia-Leal et al., 2021). Determining the associated musculoskeletal symptoms or evolutionary effects new tendencies may cause, such as the morphological changes of the hand due to chronic use of smart devices (Fuentes-Ramírez et al., 2020).

Anatomical studies have proven to be beneficial in the development of prostheses of the inferior (Adam et al., 2002) and superior limbs (Wood et al., 1989; Boileau and Walch, 1997; Pearl, 2005; Mansat et al., 2013), vertebral column screws and material (Morales-Avalos et al., 2012; Ramos-Davila et al., 2021), the development of hearing devices (Van De Water, 2012; Guzman-Perez et al., 2021), among others (Fantini et al., 2013; Negi, Dhiman and Sharma, 2014; Saunders et al., 2014). Defining the anatomy of clinical implications behind these will continue to be a valuable tool in medical development and patient safety.

ANATOMICAL EDUCATION IN A MILLENNIAL GENERATION

Currently, the millennial generation (born between 1980-1996), is the most prevalent in medical students (Ruzycki et al., 2019). New generations appear as cultural and technological changes emerge over time. It is important to understand the differences and needs of current generations in medical education, as this shared context confers a set of shared values and beliefs among generation members (Borges et al., 2006; Krebs et al., 2021). In consequence, each generation differs in career expectations, personal life, and education.

Medical education has been in a continuous adaptation to meet generational needs and maintain with technological advances, attempting to improve the education and training of future physicians. Millennials are the first ones to grow up with computer access in parallel with internet growth; they are confident with technology and prefer self-study using electronic resources. This generates a challenge, primarily for the older academic staff, due to the generation and technology (Smith, 2005; Ganguly, 2010; Eckleberry-Hunt and Tucciarone, 2011; Birden et al., 2014; Ruzycki et al., 2019). Educators must focus on assuring any technological or pedagogic tool emphasizes the core values behind medical education and professionalism (Krebs et al., 2021).

FUTURE PERSPECTIVES

Anatomical sciences are pillars of medical education. Even with the decline of anatomy hours, it is a science integrated into the curriculum, being taught at all levels as the medical student advances in their training. (Drake, 2014; Drake, McBride, et al., 2014; McBride and Drake, 2018; Salinas-Alvarez et al., 2020).

Anatomical knowledge and its application are continuous through the student evolution from a medical student to a resident, to an attendant. Its importance goes beyond the surgical specialties, although there is a clear advantage in patient safety and advancement. Evidenced-based studies must be performed.

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