Gender-specific Medicine: Yesterday’s Neglect, Tomorrow’s Opportunities

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Abstract

The Institute of Medicine has stated that analyzing data according to sex and gender may change practices used by clinicians and taught in medical education. Gender-specific medicine embraces the concept that differences between men and women encompass the entire organism, not just their reproductive biology, and that recognizing these differences will improve the precision and quality of health care for both men and women. Research conducted to date has deepened our scientific understanding of sex and gender differences in the etiology, diagnosis, progression, outcomes, treatment, and prevention of many conditions that affect both women and men.

The rapid growth and maturation of emergency medicine (EM) research provides a major opportunity to make an impact in this broad area of scientific inquiry. However, recent evidence suggests that barriers to the recognition of gender in funded and published research persist. Without systematic inclusion in research, and medical school and residency curricula, gender-based medicine cannot be translated into widespread clinical practice. Collaborations between women’s health researchers across fields of medicine will be essential, given the large knowledge deficits to be addressed and the gender-based issues that span all specialties. We provide one model for a multifaceted initiative targeting improvements in gender medicine for the specialty of EM. If emergency health services are to meet the needs of both women and men at modern-day standards, then they must acknowledge the emerging science demonstrating that sex and gender differences influence the delivery of high-quality clinical care.

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omen make up over 50% of the population and are the major consumers of health care and prescription drugs, yet historically medical research has been focused on men, with current medical knowledge and practice modeled on single-sex studies.1 Health care providers are beginning to recognize the need to improve outcomes for women and the importance of understanding the role of sex and gender in clinical practice.

We now recognize that many gender differences in medicine have the potential to affect our daily practice in the emergency department (ED). One example of a well-known sex difference is with digoxin, a medication used to treat heart failure for more than 200 years. Over the past decade, it has been discovered that digoxin therapy is associated with an increased risk of death from any cause among women, but not men, with heart failure and depressed left ventricular systolic function.2 Failure to conduct sex-specific analyses in the original trial of digoxin in congestive heart failure initially missed the significant harm of this treatment to women.

However, the available clinically relevant information on sex and gender differences in the treatment of both women and men is likely to be the “tip of the iceberg,” as gender-based investigation is a concept that has shown to have a measured effect relatively recently and still remains the exception in research studies. A review of articles published in the New England Journal of Medicine between 1994 and 1999 found that 86% of 120 trials examined did not conduct gender-specific analyses, and studies supported by the National Institutes of Health or other government funding were not more likely than studies funded by other sources to analyze results by gender.3 A review of 239 phase I and II clinical trials published in 2001 found that two-thirds of trials excluded women, and 90% did not conduct gender-specific analyses.4 Another examination of 46 federally funded U.S. clinical trials published in nine major...
journals found that 87% of studies did not report outcomes by gender or include gender as a covariate in analyses.\(^5\)

In 2010, the Institute of Medicine released a report on women’s health research that corroborated the failure to consistently include assessment of differences between men and women across all health research.\(^6\) The report identified many deficiencies in research focused on women’s health, including a lack of investigations into the social and environmental determinants of disease in women, few investigations into nonfatal but high-morbidity diseases affecting women, under-representation of socially disadvantaged groups of women, and poor communication of study findings to the women who might benefit from them. These examples suggest that there is much progress to be made in understanding the implications of sex and gender in health and disease. Further, as gender- and sex-based research findings emerge, these scientific findings will require translation into practice through medical education and training.

Emergency medicine (EM) is well positioned to take the lead in examining gender-based differences in health care. Inherently multidisciplinary, EM has come to assume a central role in health care delivery in the United States. Many individuals use the safety net of the ED as their primary point of contact with health care. EDs currently receive 120 million visits each year, or 41 patients for every 100 people in the United States.\(^7\) This number is projected to rise over the next 10 years. There are certainly challenges to incorporating gender-based practices in the ED: unlike most other health care providers, EM providers must learn to incorporate sex and gender considerations in the acute care setting, where cognitive demands are high and decision-making rapid. However, our setting is also advantageous: in the emergency setting, evidence-based practices in gender medicine may have a significant effect on a large number of patients over a short period of time. Further, EM’s comprehensive clinical realm could provide perspective on how gender-based factors might be common to diseases across different disciplines, a wealth of opportunities for collaborative gender research with other specialties, and an ideal setting to stimulate ideas about how gender-related factors may contribute to novel diagnostic or therapeutic tools.

How does EM compare to other specialties in its recognition of gender in medical research? A recent comprehensive review of EM-directed literature found that only 2% of all articles reported gender-specific outcomes, while only 10% analyzed data with gender as either a covariate or an independent variable. Twenty-one percent of the EM studies did not even report the gender of the participants\(^8\) (Figure 1). In comparison, a recent study published in the *Journal of Women’s Health* reviewed federally funded, controlled clinical trials in the top four journals for general medicine, oncology, cardiology, infectious diseases, and obstetrics and gynecology published in 2004. The study found that 7% of the 69 eligible studies did not report results by gender.\(^9\) In another review of 150 published randomized clinical trials for depression, 85% reported the sex composition of the study population and 50% reported gender-specific analysis.\(^\text{10} \) A review of cardiology clinical trials indicated that 24% of all studies reported gender-specific results.\(^\text{11} \) Although gender inclusion in all these studies remains incomplete, available data seem to indicate that EM lags behind other medical specialties in its examination of the independent effect of gender on disease.

### A Proposed Agenda for Advancing Gender-Specific EM

The 2010 edition of *Making the Grade on Women’s Health: A National and State-by-State Report Card,* conducted by the National Women’s Law Center, states that: “…the nation and the states continue to fall short in meeting women’s health needs … overall, the nation is still so far from meeting key women’s health objectives that it receives a grade of ‘Unsatisfactory’ in this fifth and last report for this decade.”\(^\text{12} \) In fact, only two states, Massachusetts and Vermont, received a “satisfactory” grade. All other states received either “unsatisfactory” or “failing.”

What can our field do to improve the understanding of gender- and sex-based factors affecting the practice of EM? It will be important to advance educational and research initiatives in concert to affect clinical practice. Formal networks of researchers and clinicians interested in gender-based science in EM may help create and promote these initiatives and increase the general awareness of the significance of sex and gender medicine within our field.

### Increasing Gender-specific Research in EM

Greater awareness of sex and gender medicine—through the increased attention of government agencies, researchers, and journal editors—has helped stimulate new perspectives on conducting research. For many, gender-based research has come to mean more than simply including women and acknowledging gender as a covariate; indeed, sampling and statistical techniques that simply adjust or control for differences in men and women fail to tell us whether the outcomes are the

![Figure 1. Percentage of studies based on a MEDLINE search of EM articles published between January 2006 and April 2009 (n = 750 articles) that reported gender composition and included gender in the study design, as an independent variable or in a primary hypothesis.\(^5\)](image)
same for men and women. Ideally, researchers will begin to routinely examine how gender modifies or mediates factors related to disease outcomes.

Increasing research focused on gender in EM will likely involve efforts on a number of fronts. First, researchers in EM should become aware of increased opportunities for federal funding of research in sex and gender differences, such as that issued by the National Institute on Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism, the Society of Women’s Health Research, and the Office of Research on Women’s Health. Formal training of EM researchers in sex- and gender-based research methods and grantsmanship will bring forth competitive applications and enable our specialty to capitalize on this expanding field of funding. Second, establishing regional and national networks of sex and gender research in EM will facilitate a shared research agenda, allowing exchange of expertise and thought processes that will advance this important subspecialty of science more efficiently. Third, researchers interested in gender questions may take advantage of existing research networks and multicenter databases such as the Emergency Medicine Network (EMNet), the Resuscitation Outcomes Consortium (ROC), or the Pediatric Emergency Care Applied Research Network (PECARN) and work with researchers to reexamine their clinical outcomes through a gender lens. Finally, collaborations between women’s health researchers across fields of medicine will be essential, given the large knowledge deficits to be addressed and the common sex- and gender-based issues that span all specialties.

Turning Research Into Education of Gender-specific EM
In 2002, the Association of Professors of Gynecology and Obstetrics (APGO) released the standard competencies and learning objectives in women’s health, which served to increase the recognition that women and men have different health care needs. Surveys of medical students and residents entering practice demonstrate that their programs lack education in gender-specific health and their examinations are void of questions that bring a women’s health perspective into the thought process. Fewer than half of the U.S. medical schools responding to a 2003 survey reported that they offer a women’s health curriculum. While 95% of these schools cover sexual and reproductive function specific to women, only a minority taught about the leading causes of death among women and medical disorders that disproportionately affect women. More recently, a 2006 study reported that 75% of medical schools had women’s health courses, but only 7% offered interdisciplinary courses that present a grounding in women’s health. Many standard medical texts still contain diagrams that show the “human abdomen” with a testicular artery, if not male genitalia. Physician training ultimately reflects what is occurring in research; as research evolves to a more gender-informed perspective, medical educators will need to change their perspective to integrate gender understanding into medical curricula and have these concepts translated into clinical practice. Fortunately, national organizations are beginning to create resources that will support educators in this effort. For example, in 2010, the Women’s Health Working Group, a joint project of the American Medical Women’s Association and the American College of Women’s Health Physicians, has launched an online virtual sex- and gender-specific research library (http://www.AdvancingWomensHealth.org). A resource by women’s health scholars across medical specialties, the site offers educational tools focused on improving women’s health and resources that will encourage physicians to recognize and apply evidence-based medicine that pertains to specific issues affecting women. The long-term goal of this collaborative effort is to introduce sex and gender medicine as a core content area in medical education, one included in medical school curricula and on all certifying examinations.

Translation of Gender-specific Medicine to Clinical Practice
Without systematic inclusion in research and medical school and residency curricula, gender-specific medicine cannot be translated into widespread clinical practice. Despite attempts to codify the existing data on gender-specific research and to create easily accessible women’s health curricula, recent findings confirm that only a small percentage of health care providers actually incorporate this knowledge into their clinical practices. Examples of ED-relevant advances in clinical research, and how these relate to patient care, include:

- According to the Drug Abuse Warning Network (DAWN), energy drink–related ED visits made by males were more likely to involve coinjection with alcohol or illicit drugs, while energy drink–related ED visits by females were more likely to involve coinjection with pharmaceuticals.
- Women are more likely to have a lower pain threshold and lower tolerance for pain than men, but data also suggest that women are more likely to be inadequately treated for their pain.
- There are fundamental gender-related differences in the nature and extent of myocardial hypertrophy and adaptation, which might account for the survival advantage for women. For example, high blood pressure in males increases the size of the left ventricle; in females the chamber does not enlarge, but the muscle of the chamber wall thickens.
- In women, aspirin has been shown to be effective in preventing stroke but not myocardial infarction (MI) or death from other cardiovascular causes; several studies have shown it to be effective at preventing MI but not stroke in men.
- Incidence and effects of musculoskeletal diseases differ between sexes. For example, women have a higher incidence of osteoarthritis and osteoporosis, and their associated complications, and sports injuries, such as anterior cruciate ligament tears.
- Women, despite being less likely to have concomitant coronary artery disease or diabetes, are significantly more likely to present to the ED with syncope, yet less likely than men to be discharged with a defined etiology.
• Men are more susceptible to sepsis, and resulting morbidity and mortality, than women; current evidence suggests immunoprotective properties of estrogen and immunodepressive properties of testosterone.23
• Female sex hormones are also thought to be neuroprotective after traumatic brain injury,24 a concept now under study in a phase III trial of progesterone infusion in patients presenting with traumatic brain injury.

Safe and effective evidence-based practice is the endpoint to which we strive as educators and practitioners. To the extent that gender is a significant factor in diagnostic reasoning and treatment decisions, all health care providers now have a shared obligation to seek a greater understanding of emerging gender-specific research findings and to provide our patients with the benefit of this evidence base by translating the science into practice.

Building an Infrastructure for Formal Training in Gender-specific EM

One model for a multifaceted initiative targeting improvements in gender medicine is provided by the Department of Emergency Medicine of The Warren Alpert Medical School at Brown University. In 2011, the department established a Division of Women’s Health in Emergency Care (WHEC). The division aims to advance and promote gender-specific research pertaining to acute health conditions, to increase advocacy and awareness for gender-based health topics, and to create educational resources and opportunities so that gender medicine may be systematically included in EM training. The division includes EM faculty members as well as a multidisciplinary and interinstitutional panel of advisors with an interest in gender medicine, including specialists in internal medicine, cardiology, adolescent health, and obstetrics and gynecology.

The Division of WHEC’s core educational and research activities include a 4-week clinical elective for third- and fourth-year EM residents, original research focused on performing gender-based analyses in a variety of EM-related clinical topics, and educational programming such as didactic sessions on gender medicine and research for the Society for Academic Emergency Medicine’s annual meeting. In recognition of the growing need for physician leaders within the field of gender-specific EM, the division developed a 2-year fellowship in Women’s Health in Emergency Care, the first program created specifically for EM physicians.25 The fellowship is a research and clinical training program designed to prepare our physicians with the skills necessary to provide gender-specific emergency care and to identify and address important research questions related to gender. The fellowship provides a focused clinical experience, opportunities to develop educational skills, training in research methods and grantsmanship, and mentored research experiences. Formal training programs such as these may bring greater national attention to this new subspecialty and create a generation of physician-scientists well prepared to contribute to research and clinical education in gender medicine.

CONCLUSIONS

New standards and guidelines have established the clear expectation that sex and gender analyses are to be considered in all areas of clinical research. Continued progress in research, if accompanied by curricular advances, should translate into improved diagnosis and treatment of both male and female patients. While all fields of medicine have been found to have gaps in their research involving gender, EM seems to lag behind other specialties, even as it provides care to a large and growing proportion of the U.S. population. If emergency health services are to meet the needs of both women and men at modern-day standards, then they should acknowledge the emerging science demonstrating sex differences influencing the delivery of high-quality clinical care. Emergency physicians have the opportunity to inform the study of gender-specific acute clinical care and are uniquely positioned to translate these types of new data into lifesaving outcomes.

Editor’s note: Academic Emergency Medicine will sponsor a consensus conference on this topic at the Society for Academic Emergency Medicine annual meeting in Dallas, Texas on May 14, 2014, “Gender-Specific Research in Emergency Medicine: Investigate, Understand, and Translate How Gender Affects Patient Outcomes” is sponsored by the Academy for Women in Academic Emergency Medicine, and co-chaired by Marna R. Greenberg, DO, MPH and Basmah Safdar, MD.

References


