What Is the Global Burden of Unsafe Medical Care?

Jha A, Larizgoitia I, Audera-Lopez C, et al. The global burden of unsafe medical care: analytic modeling of observational studies. BMJ Qual Saf 2013;22:809-15.

Study Overview

Objective. To examine the global burden of unsafe medical care and its comparative frequency in low/middle-income vs. high-income countries.

Design. Analytical modeling of aggregated data from observational studies.

Data. Two primary sources of data were used. First, the team conducted a search of over 16,000 articles written in English after 1976 that aimed for a comprehensive examination of both peer-reviewed and non–peer-reviewed studies that focused on 7 inpatient adverse events (see below), and the clinical features of the patients who were injured from them. Two separate literature reviews were conducted in 2007 through early 2008 and then repeated in 2011. Discussions with international experts in each topic area informed the selection process. The second source of data was epidemiological studies commissioned by the World Health Organization (WHO). These aimed to identify inpatient adverse events using a 2-stage medical record review in 26 hospitals across 8 low- and middle-income countries (LMICs) in the Eastern Mediterranean and North African regions, and 35 hospitals across 5 countries in Latin America.

Main outcome measures. 7 types of adverse events were evaluated in the analysis: (1) adverse drug events, (2) catheter-related urinary tract infection, (3) catheter-related blood stream infections, (4) nosocomial pneumonia, (5) venous thromboembolism, (6) falls, and (7) pressure ulcers (decubiti). The global burden of disease (GBD) is a standard metric that uses disability-adjusted life years (DALYs) as a proxy measure of morbidity and mortality related to a specific condition. The GBD DALYs model requires several key inputs: the number of people affected, the age at which they are affected, and the clinical consequence of the adverse events. In this study, a single average age per event was used instead of the standard GBD calculations by age and sex. Each input of GBD and DALYs was calculated separately for high-income countries (HICs) versus LMICs. The World Bank sets the income categorization for countries and adjusts the information on an annual basis. Countries in each category share common characteristics of socioeconomic development and epidemiological profiles.

Main results. The rate of hospitalization in HICs was higher than in LMICs: 10.8 vs. 3.7 per 100 citizens per year. There were large variations in the reported incidence of adverse events in both HICs and LMICs. Of the 7 adverse events assessed, adverse drug events

were the most common type in HICs, with an incidence rate of 5.0%. In LMICs, venous thromboembolism was most common, with an incidence rate of 3.0%. Catheter-related blood stream infection, venous thromboembolism, and pressure ulcers had comparable rates between HICs and LMIC . The authors estimated that for every 100 hospitalizations, approximately 14.2 adverse events in HICs and 12.7 in LMICs. This is roughly 16.8 million injuries annually among hospitalized patients in HICs. LMICs and experienced approximately 50% more adverse events than HICs. Of note, LMICs had 5 times the population of HICs but the authors did not calculate proportional incidence rates.

The authors estimated 22.6 million DALYs lost due to these adverse events in 2009 globally. Unsurprisingly, the number of DALYs lost were more than twice as high as in LMICs as they were in HICs. This is likely due to the combination of weaker health systems and human resources for health shortages in those countries. In LMICs, venous thromboembolism was the main source of lost DALYs. Although incidences of hospital-acquired infections--such as nosocomial pneumonia, catheter-related blood stream and urinary tract infections--were smaller, they caused a comparable number of DALYs lost. Premature death from adverse events was the primary source of DALYs lost for all countries.

Conclusion. Adverse events from unsafe care is a significant problem across all countries.

Commentary

Globally, the efforts to improve health care delivery for diseases that cause substantial morbidity and mortality have been largely successful. For example, antimalarial drugs and antiretroviral therapies have become more accessible to patients in need [1,2]. However, in order to create more sustainable model, the health care systems of developing countries need sustainable investments to care for their growing populations and increasing medical needs [3,4]. Allengranzi et al [5] concluded from a systemic review that health care–associated infections are ubiquitous and occur at much higher rates in LMICs than in HICs. Findings from this study support those from Allengranzi's review.

This study helped further our understanding of and explored the impact of unsafe medical care on GBD and DALYs. Several other adverse events related to unsafe care, such as unsafe surgery, harms due to counterfeit drugs, unsafe childbirth and unsafe blood use, were not included in this study due to data limitations. The estimated lost DALYs would be much higher if these events were counted.

This study has several strengths. First, the authors sought out the best available data from a large number of sources. Evidence selected for the analysis came from studies with good quality ratings. The 7 outcome measures used in this study are now standard minimum reporting data internationally. Nonetheless, several limitations are present. As the authors noted, the lack of availability high-quality data is common in international analyses. There can be reporting delays, data collection errors due to a lack of technical capacity, and corruption problems that may influence data quality. Poor reporting practices may exclude or underreport adverse events. Also, the paucity of data for some variables limited the calculation of estimates Second, few studies used standardized approaches in their data collection and analysis, contributing to data inconsistencies that may affect the reliability of the results. Third, the same life expectancy value (the WHO standard) was used for all individuals regardless of their countries' life expectancy. The authors acknowledged that this approach was controversial and may have resulted in a different number of DALYs lost. Finally, only English-language publications were used, which may have influenced the findings. Latin America, the former Soviet Union states, and many Asian countries have growing bodies of research published in their native languages.

Despite the limitations, the study is one of the first systematic analyses of GBD, the outcomes of unsafe medical care, and associated lost DALYs. The analysis identified that a majority of the harms from adverse events occur in LMICs. Policies addressing, supporting, and enforcing patient safety measures during the health care experience will help ensure reductions in mortality and morbidity in LMICs. Improving the safety of the healthcare system should be a major policy and research emphasis across the globe.

Applications for Clinical Practice

Even though patient safety initiatives have been at the forefront of many organizational policies and health care provider education since the 1999 Institute of Medicine report "Crossing the Quality Chasm," this study reminds practitioners that safe clinical practice is essential for reducing domestic disease burden. The cost of

adverse events from unsafe practice in the United States was estimated to be around $16.6 billion in 2004 alone [6]. With the World Health Organization calling for strengthened research infrastructure across the globe and LMICs now seeing the value of data for health systems policymaking and management, future research will help to further refine the methods developed in this study.

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Does Bioelectrical Impedance Analysis Provide a Reliable Diagnosis of Secondary Lymphedema in Breast Cancer Patients?

Fu MR, Cleland CM, Guth AA, et al. L-dex ratio in detecting breast cancer-related lymphedema: reliability, sensitivity, and specificity. Lymphology 2013;46:85-96.

Study Overview

Objective. To evaluate the reliability, sensitivity, and specificity of bioelectrical impedance analysis (BIA) in the diagnosis of secondary lymphedema.

Design. Cross-sectional study utilizing test-retest method

Setting and participants. The researchers used a purposeful sampling technique to recruit women between 2010 and 2011 from a metropolitan cancer center and communities in the New York City metropolitan area. Participants included women who were 18 years of age or older and able to read and write in English. Exclusion criteria included patients with bilateral breast disease, recurrent cancer, artificial limb, knee, or hip, and kidney or heart failure. Study participants were divided into 3 groups: breast cancer survivors with lymphedema, those at risk for lymphedema, and healthy adult women (no history of breast cancer or lymphedema). Women in the at risk category had to have completed surgical treatment, chemotherapy and/or radiation within the 5 years prior to the study enrollment.

Measurements. Patient's arms were measured by the same 2 researchers using sequential circumferential measurements. BIA was measured in all patients with the ImpXCA (Impedimed Inc, Pittsford, NY), an FDA-approved device that measures impedance and resistance of the extracellular fluid. The ImpXCA utilizes a scale to correlate BIA to an L-Dex (lymphedema index) ratio; –10 to +10 defines the normal range of L-Dex values for a patient without lymphedema. Measurements were taken at 5-minute increments for a total of 3 times at the same visit to test for stability of BIA.

Main results. 250 patients were in the sample: 42 with known lymphedema, 148 at risk for lymphedema, and 60 healthy female adults. L-Dex ratios ranged from –9.7 to 7.7 in the healthy population, –9.6 to 36.9 in the at risk group, and 0.9 to 115 in the group with lymphedema. Mean L-Dex ratios were significantly different between

the healthy and lymphedema groups ($P < 0.001$) and the at risk and lymphedema groups ($P < 0.001$). There was no difference between the at risk and healthy groups ($P = 0.85$). Utilizing an L-Dex ratio cutoff of 7.1 provided 80% sensitivity and 90% specificity in the diagnosis of secondary lymphedema.

Reliability and reproducibility of BIA by ImpXCA using the L-Dex ratio was assessed using a test-retest method. Intra-class correlation coefficients (ICC) provided strong stability for the repeated measurements in the healthy group, with ICC = 0.99 (95% CI, 0.99–0.99), and in the at risk group, with ICC = 0.99 (95% CI, 0.99–0.99). There was also fair agreement in the repeated measurements in the lymphedema group, with ICC = 0.69 (95% CI, 0.58-0.82). All of these findings were statistically significant ($P < 0.001$).

Conclusion. The L-Dex ratio is reliable and reproducible and may be helpful in distinguishing women with lymphedema from those without lymphedema. BIA in conjunction with other tools, such as self-report of symptoms, circumferential measurements, and clinical observation, may have a role in diagnosing lymphedema.

Commentary

The first year and a half following surgical treatment for breast cancer is when providers tend to diagnose the initial onset of lymphedema [1]. Many women, however, go undiagnosed until the illness has progressed. Earlier treatment has the potential to improve patient outcomes [2]. Although awareness of secondary lymphedema among breast cancer survivors has increased over the past 10 years, the diagnosis remains difficult and the development of effective diagnostic tools continues to challenge health care providers.

The current gold standard for diagnosis is the water displacement method where the affected and unaffected extremities are each placed into a tank of water, and the displaced water is measured [3]. Greater than a 200 mL discrepancy between arms is used to make a diagnosis of lymphedema. While useful, this measurement is messy and difficult to set up, and thus underutilized. Many providers have turned to circumferential measurements as their primary method to diagnose and monitor lymphedema [4]. However, this method may miss patients in the earlier stages of lymphedema, since it measures the size of limbs rather than changes in the tissue. Without a definitive test to diagnose lymphedema, researchers and health care providers continue to search for the most accurate, reliable, and feasible means to assist in the diagnosis.

This cross-sectional study suggests that L-Dex can be helpful in detecting lymphedema. A weakness of the study is that the investigators did not compare the results of BIA to the current gold standard of water displacement, but rather to circumferential measurement. In addition, while all results were reproducible, the difference between groups was notable in terms of age and body mass index, making it difficult to generalize to all patients at risk for lymphedema or differentiate results by those same variables. Although having the same 2 investigators obtain circumferential tape measurements is preferable to having multiple investigators do so, such measurements are still at risk for human error.

BIA shows promise as a diagnostic tool. Future studies should include healthy patients with characteristics similar to those of at risk patients and lymphedema patients. Efforts also could be directed towards determining whether combining BIA with other methods, such as self-report, circumferential measurements, and close observation, may offer greater sensitivity and specificity than one method alone.

Applications for Clinical Practice

Secondary lymphedema is a common complication caused by surgical treatment of breast cancer. Early treatment is linked to a decrease in debilitating factors such as immobility of affected joints, skin changes, and risk for infection. Measurement of extracellular fluid utilizing L-Dex ratios produces reliable and repeatable results in the assessment for lymphedema. Paired with additional tools and resources it may be helpful in making a diagnosis, which is normally difficult in its earliest stages. The early diagnosis of secondary lymphedema may allow for improved quality of life for survivors of breast cancer.

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