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Sex differences and in-hospital outcomes in patients undergoing mechanical circulatory support implantation

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sex;
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BACKGROUND: Mechanical circulatory support (MCS) is a widely available management strategy. No studies have described sex differences in both extracorporeal and durable MCS. We analyzed sex-related differences of in-hospital outcomes for extracorporeal and durable MCS using administrative hospital data.

METHODS: In total, 134.5 million hospital records between 1994 and 2012 were screened for placement of MCS using procedure codes of the International Classification of Diseases-9, Clinical Modification. Major adverse events (MAEs) were defined as death, major bleeding, stroke, device infection or mechanical complication. Participation in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) registry was determined on an annual basis using quarterly reports of the INTERMACS. Associations between characteristics and outcomes were determined using multivariable logistic regression.

RESULTS: Sex was reported in 3,523 of 4,337 patients undergoing MCS placement from 45 INTERMACS sites ($n = 1,383$) and 246 non-INTERMACS sites ($n = 2,954$). Twenty-two percent were female. Baseline characteristics were significantly different with women being slightly younger (33.5% vs 27.4% age <50 years, $p < 0.001$; mean 55.7 ± 17.3 vs 56.1 ± 14.6 years) with fewer comorbidities. Women had higher rates of in-hospital mortality (52.3% vs 40.8%, $p < 0.001$) and MAEs (64.8% vs 52.5%, $p < 0.001$). Women had an 89% higher likelihood of MAEs when corrected for multivariate predictors ($p < 0.001$). In-hospital mortality decreased over time for both men and women (10% relative risk reduction/year, $p < 0.001$), but mortality in women was higher than in men throughout the study period.

CONCLUSION: There are significant sex differences in characteristics and outcomes of patients receiving MCS. Women had higher in-hospital mortality and were at increased risk of MAEs, which could not be explained by age or comorbid conditions. Further research on the causes of these disproportionate outcomes is needed.

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Mechanical circulatory support (MCS) made its debut in the 1950s to support cardiac surgery.[1,2] Significant advances have been made since that time including the development of durable continuous-flow devices, such as the HeartMate II (Thoratec, Pleasanton, CA) and HVAD (HeartWare, Framingham, MA)

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left ventricular assist devices (LVAD). Major sex differences in survival and outcomes have been described for other cardiac surgeries,[3–5] and the exponential rise in the use of short- and long-term MCS in the United States emphasizes the need to track sex differences in use and outcomes.[6–8] The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), established in 2005, is a prospective registry that collects clinical data from pre-implant through the recipient's remaining lifespan.[9] The most recent INTERMACS statistics show that from June 23, 2006 through September 30, 2015, women accounted for 21.2% ($n = 3{,}254$) of all MCS.[9] Although INTERMACS is an expansive repository, it relies upon voluntary hospital participation and manual data entry. Further, data only date back to 2006 when 15 hospitals participated in the registry, and a large percentage of MCS devices are placed in non-INTERMACS sites. Hospital record data have been made publicly available in several states dating as far back as 1994. Herein, we report sex-related differences of both extracorporeal and durable MCS devices and associated outcomes using administrative hospital data.

Methods

This analysis was approved via exemption by the Colorado Multiple Institutional Review Board. De-identified hospital discharge data were obtained from California (2000 to 2011),[10] New York (1994 to 2007),[11] New Jersey (1997 to 2011),[12] New Hampshire (1999 to 2007),[13] West Virginia (2003 to 2007),[14] Colorado (2006 to 2012)[15] and Texas (1999 to 2008).[16] We included hospital encounters that reported MCS implantation defined as International Classification of Diseases-9, Clinical Modification (ICD-9 CM) Procedure Codes 37.60 (simultaneous biventricular external assist device [BiVAD]), 37.62 (temporary ventricular assist device [VAD]), 37.65 (single ventricle extracorporeal VAD) or 37.66 (implantable VAD). All patients' demographics and admission characteristics were determined using data set documentation.

Hospital participation in the INTERMACS registry was determined on an annual basis using quarterly INTERMACS summary reports. Specifically, hospitals submitting cases to the INTERMACS registry during the fourth quarter of a calendar year were considered to be active INTERMACS sites for that year. INTERMACS reporting status was set as a categorical covariate in subsequent analyses.

The primary outcome for this study was a major adverse event (MAE), defined as death, significant bleeding (intracerebral hemorrhage, hemorrhagic cystitis, hematemesis, throat hemorrhage, epistaxis, gastrointestinal hemorrhage not otherwise specified, hematuria, intraperitoneal hemorrhage or variceal bleeding), stroke, device infection, or mechanical device complication. Secondary outcomes included in-hospital death, length of stay and discharge to home versus sub-acute care, such as skilled nursing facilities.

Statistical analysis

The primary covariate of interest was sex. Associations between outcomes and patient demographics, comorbidities, route of admission, year of hospitalization, acute presentation diagnoses and INTERMACS report status were modeled using step-forward multivariable logistic regression. All patients' characteristics with a chi-square p-value of <0.05 between patients with and without an adverse event or a Mann–Whitney U-test p-value of <0.05 for length of stay were included in univariate, then multivariable logistic regression for MAE and death and Poisson regression analysis for length of stay. A univariate $p < 0.05$ was used as the entry criterion for multivariable analysis. Data harmonization was performed using MySQL Server (version 5.5.24, Oracle Corporation, Redwood City, CA). Statistical analyses were performed using R statistical software (version 3.1.1, R Foundation for Statistical Computing, Vienna Austria). $p < 0.05$ was considered significant throughout.

Results

Study population demographic and clinical characteristics

Between 1994 and 2012, 4,337 patients undergoing MCS were identified from approximately 134.5 million hospital discharge records. Due to state-specific de-identification practices, sex was reported in 3,523 cases, with the majority of missing data arising from California (775 of 1,509 missing sex). Overall 1,383 of 4,337 (31.9%) MCS procedures were performed at sites during participation in the INTERMACS registry. Trends in sex distribution of MCS are found in Figure 1. Women made up a minority (22%) of MCS recipients throughout most of the study period with the exception of the first 2 years when procedure volume was low (≤ 20 procedures).

Demographic and clinical characteristics of MCS recipients stratified according to sex are presented in Table 1. Women were younger (33.5% vs 27.4% age <50 years, $p < 0.001$) and less likely to be white ($p < 0.001$). Women also had less atrial fibrillation, coronary artery disease, coronary artery bypass grafting and acute renal failure compared with men. A significantly higher percentage of women underwent simultaneous BiVAD, extracorporeal VAD and extracorporeal membrane oxygenation (ECMO)

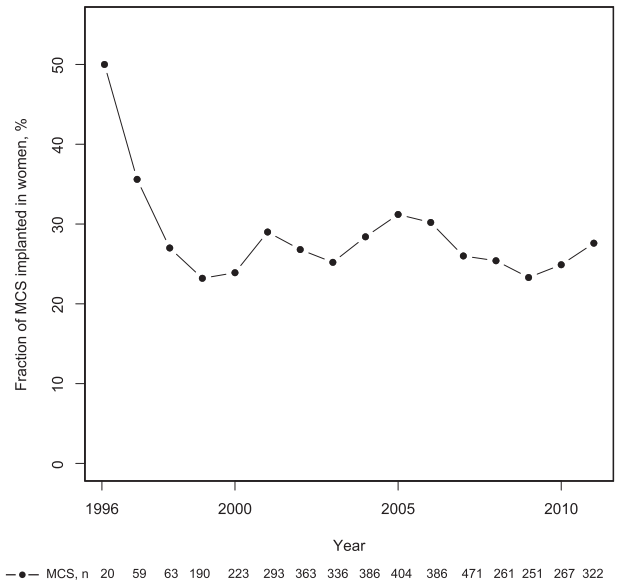

Figure 1 Fraction of mechanical circulatory support implanted in women over time.