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## Sensitivity of Current Methods for Diagnosing and Documenting Metabolic Syndrome Within a Large Community-Based Health Care System

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# Conference Proceedings: Aurora Scientific Day 2017

The following abstracts were presented at the 43rd Annual Aurora Scientific Day research symposium, held May 24, 2017, in Milwaukee, Wisconsin. Aurora Scientific Day hosts a forum for original research conducted by faculty, fellows, residents, and other allied health professionals affiliated with Aurora Health Care, an integrated health system with hospital and clinic locations in eastern Wisconsin and northern Illinois.

## **FIRST PLACE POSTER**

### **Assessment of Chronic Disease to Determine Appropriateness of Implantable Cardioverter-Defibrillator Therapy**

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**Background:** Implantable cardioverter-defibrillator (ICD) therapy is considered appropriate when a patient is felt to have a reasonable expectation of 1-year survival. Chronic diseases have been estimated to be associated with greater than 10% annual mortality and may reduce benefits of ICD therapy. Frailty has been estimated to be associated with greater than 20% annual mortality and has been suggested to contraindicate ICD therapy.

**Purpose:** Determine a risk score that may identify patients in whom ICD implantation may not be appropriate.

**Methods:** Patients who received an ICD for primary and secondary prevention from 2008 through 2013 at the Aurora Health Care network were studied retrospectively. Using Cox regression, a scoring system based on hazard ratios was devised to reflect risk associated with comorbidities. Survival was evaluated by Kaplan-Meier estimates.

**Results:** The study cohort includes 1,558 patients (mean age: 61.3 years; 495 female). Comorbidities associated with mortality included in the risk score were need for hemodialysis, myocardial infarct within 3 months prior to ICD implantation, sustained monomorphic ventricular tachycardia, New York Heart Association functional class III, age greater than 70 years, intraventricular conduction delay, diabetes mellitus, and chronic lung disease. A risk score of greater than or equal to 6 was associated with 10% mortality at 1 year and more than 20% mortality by 2 years.

**Conclusion:** Chronic comorbidities have a cumulative effect on mortality. Using our scoring system, patients with a risk score of 6 or greater have at least 10% mortality at 1 year and more than 20% mortality by 2 years.

## **SELECT ABSTRACTS**

### **Sensitivity of Current Methods for Diagnosing and Documenting Metabolic Syndrome Within a Large Community-Based Health Care System**

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**Background:** Metabolic syndrome (MetS) is a constellation of metabolic conditions, including abdominal obesity, high blood pressure, high triglyceride level, low high-density-lipoprotein level and high fasting blood glucose level, that increase the risk of developing chronic health conditions. Various combinations of diagnostic criteria have been proposed, including those by the National Cholesterol Education Program Adult Treatment Panel III (ATP III), World Health Organization (WHO) and International Diabetes Foundation (IDF), among others. However, inconsistent use of diagnostic criteria and inadequate scientific evidence supporting use of specific criteria are current problems in health care.

**Purpose:** Quantify the prevalence of MetS diagnosis within the Aurora Health Care patient population and determine the sensitivity (ie, accuracy) achieved in documenting MetS within Aurora, recognizing ATP III, WHO and IDF definitions of MetS as diagnostic gold standards.

**Methods:** We conducted a retrospective review of all patients encountered within Aurora from January 1, 2012, to December 31, 2015. Patients were examined to determine the occurrence and associated dates of MetS diagnosis and all indications of satisfied MetS diagnostic criteria. Indications of obesity, hyperglycemia, hypertriglyceridemia, hypoalbuminemia and hypertension, as variably defined in ATP III, WHO and IDF guidelines, included relevant diagnoses, abnormal clinical and laboratory test results and use of medications. Sociodemographic data also were collected.

**Results:** In total, 1,369,620 unique patients visited Aurora during the study period, with 28% of patients aged  $\geq 60$  years and most identifying as non-Hispanic white (76.8%) or black (9.93%) race. Only 4,978 patients (0.36%) received a clinical diagnosis of MetS despite evidence of satisfied ATP III and WHO criteria in 12.0% and 16.7% of patients, respectively. Satisfaction of IDF criteria occurred in only 0.16% of patients. Except for hyperglycemia, individual diagnostic criteria also showed lower-than-expected rates of clinical diagnosis. For example, obesity was diagnosed in 7.86% of patients but suggested in 39.3% of patients with body mass index  $\geq 30$  kg/m<sup>2</sup>. The true positive rate (ie, percentage of patients with satisfied criteria who also were clinically diagnosed) was lowest in older, male, black or Hispanic patients.

**Conclusion:** Within Aurora, metabolic syndrome is rarely and variably diagnosed in medical practice, despite clear evidence of satisfied ATP III and WHO criteria.

### Improved Service Efficiency Improves Racial Disparity in Diabetic Care

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**Background:** Racial disparities in diabetes care have been documented. Disparities also have been shown to affect service quality and outcome of diabetic care. Analysis of our internal medicine residency clinic diabetic care management performance across REAL-G (race, ethnicity, age, preferred language and/or gender) showed race-based disparity on two outcome measures: 1) measurement of glycohemoglobin (A1C) at least twice a year; and 2) target blood pressure of < 140/90.

**Purpose:** Develop interventions to decrease racial disparities in diabetes care among patients managed by an internal medicine residency clinic, as part of the Alliance of Independent Academic Medical Center's National Initiative V project.

**Methods:** Interventions were developed following analysis of clinic performance data by REAL-G categories, workflow analysis and multidisciplinary clinic team meetings. A point-of-care A1C machine was procured and workflow developed using the Plan-Do-Study-Act cycle. Staff training was conducted. A rolling 12 months data set was obtained from electronic health records. Baseline data range was December 2014 to November 2015, while endline data were from January 2016 to December 2016. The interventions were launched in July 2016. Percentage difference between baseline and endline outcome indicators was calculated and Z-score test assessed. Statistical significance was set at  $P < 0.05$ .

**Results:** At baseline, 62.9% (401 of 638) of patients who self-identified as African American/black (AA) had A1C measured at least twice a year compared to 74.3% (107 of 144) of patients who self-identified as white/Caucasian (WC), a percentage difference of 11.4% ( $P=0.01$ ). For goal blood pressure in diabetics, 71.0% (453 of 638) of AA met the target as compared to 80.6% (116 of 144) of WC, a percentage difference of 9.6% ( $P=0.003$ ). Following the intervention, a higher percentage of AA patients (71.4% [381 of 534]) had at least two A1C measured during project period. The outcome also showed improvement for WC (79.8% [95 of 119]). The percentage difference between races narrowed to 8.5% ( $P=0.06$ ). For goal blood pressure, 75.1% of AA achieved the target compared to 81.5% of WC, with percentage difference narrowing to 6.4% ( $P=0.14$ ).

**Conclusion:** Racial disparities in diabetes were confirmed, even for a clinic setting in which black patients are predominant. Racial disparity can be improved by implementing interventions that improve service for all patients.

### Generation of a Patient-Derived Brain Metastasis Breast Cancer Cell Line via Novel Orthotopic Injection Placement and Serial Mouse Transplantation to Develop PDF Mouse Model

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**Background:** The incidence of brain metastasis appears to be increasing, potentially due to advanced technology that aids early diagnosis. Patient-derived xenografts (PDX) have high translational value, as these models retain key functional characteristics of the patient tumor. PDX models are useful to understand the molecular basis of tumorigenesis and to identify new treatment targets. However, generating a first-line PDX model is challenging as engraftment failure is high. Serial transplanting tumor tissue via mouse-to-mouse propagation increases engraftment rates and decreases PDX development time. Herein we report methods to generate a PDX cell line from patient-derived tumor tissue that includes the cerebral aqueduct as a novel intracranial orthotopic implantation site.

**Purpose:** Develop human tumors in mouse models for therapeutic purpose.

**Methods:** Patient-derived brain metastasis tumor tissue was enzymatically dissociated into a single cell suspension and maintained in neurocult media supplemented with human recombinant bFGF and EGF (20 ng/ml). The cells were seeded at a density of  $1.0 \times 10^4/\text{cm}^2$  on ultra-low attachment plates and maintained at 37°C with 5%  $\text{CO}_2$ . PDX models were generated via orthotopic stereotactic surgeries. Athymic nude mice were anesthetized with an intraperitoneal injection of ketamine (100 mg/kg) and xylazine (10 mg/kg). The cerebral aqueduct was located using these coordinates from bregma: A: -5; L: +0.2; V: -2.4. Mice were injected with  $5.0 \times 10^4$  cells in 2  $\mu\text{l}$  of media at a rate of 0.4  $\mu\text{l}/\text{min}$ . Mice were monitored daily for symptoms of tumor formation. Upon becoming symptomatic, mice were euthanized and tumor tissue was harvested for both culture and H&E stain for tumor verification.

**Results:** Mice injected with primary patient cells (first-generation mice) developed tumors at 7 weeks (average: 6.77 weeks), second-generation mice yielded tumors at 2 weeks (average: 13.5 days), and third-generation mice replicated results from second-generation mice (average: 13 days). H&E stain revealed invasive tumor masses in the ventricular system that extended from the cerebral aqueduct to the lateral ventricles. Immunohistochemistry analysis confirmed the third-generation cell line retained key characteristics of the patient tumor.

**Conclusion:** These methods successfully generated a PDX cell line from patient-derived brain metastasis that demonstrates reliable tumor formation and phenotypic stability. Importantly, our unique intracranial implantation site revealed several distinct masses, a hallmark of brain metastasis in patients.

### Decreasing Time to Broad Spectrum Antibiotics for Septic Patients in the Emergency Department

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**Background:** Timely administration of broad spectrum antibiotics has been shown to be directly correlated with decreased mortality for patients with severe sepsis and septic shock. As such, both the Surviving Sepsis Campaign and the SEP-1 CMS measure recognize timely antibiotic administration as a cornerstone of therapy for patients with severe sepsis or septic shock.

**Purpose:** Decrease time to broad spectrum antibiotic administration for septic patients in the emergency department (ED) of Aurora St. Luke's Medical Center.

**Methods:** An alert within the electronic medical record was created to more rapidly identify potentially septic patients in the ED. After