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Prediction of quality of life improvements in patients with lumbar stenosis following use of membrane stabilizing agents☆

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ABSTRACT

Objective: Membrane stabilizing agents (MSAs) improves function and reduces neuropathic pain in a subset of patients with LSS. No study has investigated the pre-treatment demographic and psychosocial factors associated with quality of life (QOL) outcomes following the use of MSAs. In this study we sought to create prediction models for post-treatment outcome.
Methods: All patients who were diagnosed with LSS and treated with MSAs at a single institution between September 2010 and March 2013 were retrospectively reviewed. QOL outcomes were collected prospectively. Prediction tools were created using multivariable logistic regression and Cox proportional hazard models. Outcome measures were: 1 – need for surgery within 1 year after initiating MSA treatment, 2 – time until surgery after initiating MSA treatment, 3 – any improvement in EuroQol (EQ)-5D QOL index, 4 – improvement in EQ-5D index exceeding the minimum clinically important difference (MCID).
Results: 1346 patients were included. For goal 1 (need for surgery), the prediction model was less robust. For goal 2 (time to surgery), only age was a significant predictor, with each 10-year increase in age causing the hazard of eventually having surgery to increase by 20%. 382 patients were available for analysis for goals 3 and 4 (predicting improvement in EQ-5D). Prediction models for these goals were good with *C*-statistics 0.73 and 0.85, respectively. Predictive factors for superior outcomes included lower baseline EQ-5D index (worse QOL), less baseline depression, greater median income, and being married.
Conclusion: MSA treatment provides improvements in quality of life for those individuals with LSS. Treatment effects of MSAs will be greatest in those with worse quality of life, less depression, married patients, and those of higher socio-economic status.

1. Introduction

The physiologic degeneration of the spine that occurs with age can often lead to the pathologic state of lumbar spinal stenosis (LSS). A common disease process that increases from approximately 20–50% [1] of all patients between ages of 40 and 60, LSS will become increasingly prevalent in the United States as the population continues to age. Patients with LSS can present with radicular, claudicant, or myelopathic symptoms. When refractory to conservative management, patients with symptomatic LSS may be treated via surgical decompression with or without the addition of fusion. Identifying those patients most likely to benefit from conservative therapies and optimizing non-operative treatment will minimize the risk of surgical morbidity and potentially reduce health-care costs.

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The mainstay conservative therapies have traditionally included physical therapy, epidural injections, analgesics, and anti-inflammatory medications. While currently off-label, membrane stabilizing agents (MSAs), such as gabapentin (Neurontin, Pfizer, New York) and pregabalin (Lyrica, Pfizer, New York), have been shown to be effective in improving function and reducing neuropathic pain associated with LSS [2–4]. While they have the potential to substantially improve quality of life (QOL) and limit the need for surgery, MSAs also have inherent risks, side effects, and added costs. No study has investigated the pre-treatment demographic, QOL, and psychosocial factors associated with outcomes following the use of MSAs. Therefore, we sought to create prediction models for LSS patients treated with MSAs for the following outcomes: 1 – need for surgery within 1 year after initiating MSA treatment, 2 – time until surgery after initiating MSA treatment, 3 – any improvement in EuroQol (EQ)-5D QOL index (i.e., post-treatment score – pre-treatment score > 0), 4 – improvement in EQ-5D index exceeding the minimum clinically important difference (MCID).

2. Methods

2.1. Study sample

A retrospective study was performed of all patients who were diagnosed with LSS at a single tertiary-care institution between September 2010 and March 2013. Patients that received an MSA were identified. Patients received additional conservative management based on the discretion of the health care provider. The electronic medical records were queried to retrieve patient data that fit our criteria.

Included patients were greater than 18 years old with a diagnosis of LSS, which would be made based on specific criteria, such as gluteal and/or lower extremity pain and/or fatigue with or without back pain, symptoms aggravated by upright exercise, such as walking or position-induced neurogenic claudication, and symptomatic relief with forward flexion, sitting, or recumbency. Inclusion was also dependent on participation in the institutional prospectively maintained database collecting QOL outcomes measures. Exclusion criteria included previous spinal surgery, previous treatment with a MSA for any disease, spinal tumors, cauda equina syndrome, foot drop, spinal fracture, epilepsy, and renal failure.

2.2. Quality of life outcomes

Quality of life (QOL) outcomes data included Patient Health Questionnaire-9 (PHQ-9) [5–7] and EuroQOL-5 Dimensions (EQ-5D) [8–10] and were acquired via the institutional Knowledge Program (KP). The KP is a patient derived outcome assessment tool that is embedded in our electronic medical record. These data have been systematically collected in the Center for Spine Health since 2009, in a prospective fashion, at each outpatient encounter. All patients must have had an outpatient visit to the Spine center no more than 30 days before starting MSA treatment in order to have pre-treatment data. For the post-treatment QOL data, we chose the visit closest to 6 months. For patients that eventually underwent surgery, post-treatment QOL data was obtained prior to the surgery date.

The PHQ-9 is a self-administered assessment for depression in patients that evaluates the 9 DSM-IV criteria for major depressive disorder. Each of the 9 questions is scored from 0 ("not at all") to 3 ("nearly every day"), making the total score range from 0 to 27. The total score is commonly categorized into one of five groups: minimal (score = 0–4), mild (score = 5–9), moderate (score = 10–14), moderate-severe (score = 15–19), and severe (score = 20–27). The diagnostic validity of the PHQ-9 has been established in large multicenter analyses [5,6]. The EQ-5D contains five dimensions of health state: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (A/D). Each dimension is scored from 1 to 3. The minimum clinically important difference (MCID) used for EQ-5D was 0.1 [11,12]. This MCID value is further supported by method described by Norman et al. [13] using half the baseline standard deviation for the EQ-5D index.

2.3. Statistical methods

Summary statistics (e.g., means, standard deviations, frequencies, percentages) were calculated for all eligible patients and stratified by whether patients had a follow-up visit with EQ-5D data between 2 months and 1 year after starting MSA treatment. Comparisons were made using *t*-tests for continuous variables and chi-square tests for categorical variables.

For the prediction models in goals 1, 3, and 4, we created multivariable logistic regression models where the outcomes were (1) had surgery within 1 year after starting MSA (yes vs. no), (3) >0 improvement in EQ-5D index (yes vs. no), (4) $\geq$0.1 improvement in EQ-5D index (yes vs. no). For goal 2, a Cox proportional hazards model was created. For all 4 models, the pre-treatment predictors included were patient age, gender, marital status (not married vs. married), insurance status (Medicare/Medicaid vs. private/other), household median income by patient zip code, pre-treatment EQ-5D index, and pre-treatment PHQ-9 score. The models were created and validated using the rms package, version 4.0-0, in R version 3.0.1. Validation was done using bootstrap methods with 200 iterations. Multiple imputation [14] was used to handle missing data. Model discrimination was checked using the *C*-statistic (concordance statistic, which is equivalent to the area under the receiver operating characteristic curve). Calibration, a measure of how well the model's predictions matched the observed outcomes, was checked graphically (see reference for further explanation regarding calibration and discrimination [15]). For the Cox proportional hazards model in goal 2, surgery status was considered known until the last visit date in the electronic medical records. Thus, patients that did not have surgery on or before the last date were considered censored.

3. Results

There were 1346 patients that met inclusion criteria. Table 1 displays summary statistics for the entire cohort as well as patients that were and were not included in the analyses for goals 3 and 4. Of the 1346 patients in the entire cohort, 1030 took only gabapentin during the study, 145 patients took only pregabalin, and 171 took both.

Of the 1346 patients included in the study, 1087 (80.8%) completed the EQ-5D at their pre-treatment visit. However, only 382 (28.4%) also had an appointment between 56 and 365 days after treatment where the EQ-5D was completed and, thus, were included for analyses in goals 3 and 4. There were some differences between the groups of patients that were and were not included in the analyses for goals 3 and 4. Patients that were included in these analyses were more likely to have taken both MSAs during the study rather than just one. Patients included were also more likely to be Caucasian, married, and have private insurance or have an unknown insurance status.

3.1. Goal 1: need for surgery within 1 year after initiating MSA treatment

Of the 942 patients that had sufficient follow-up time, 99 (10.5%) had surgery within one year of starting MSA treatment. Table 2 displays the results for the model predicting surgery within one year