International Journal of Cardiology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Incidence and outcomes of cardiac tamponade in patients undergoing cardiac resynchronization therapy

Oluwole Adegbala [a,*], Olakanmi Olagoke [b], Adeyinka Adejumo [c], Emmanuel Akintoye [d], Adegbola Oluwole [e], Prince Alebna [a], Karlene Williams [a], Randy Lieberman [d], Luis Afonso [d]

[a] Department of Internal Medicine, Englewood Hospital and Medical Center, Seton Hall University-Hackensack Meridian School of Medicine, Englewood, NJ, United States of America
[b] Department of Medicine, John H Stroger Jr. Hospital of Cook County, Chicago, IL 60612, United States of America
[c] Department of Internal Medicine, North Shore Medical Center, Salem, MA, United States of America
[d] Division of Cardiology, Wayne State University/Detroit Medical Center, Detroit, MI, United States
[e] Department of Internal Medicine, Einstein Medical Center Philadelphia in Philadelphia, PA, United States of America

ARTICLE INFO

Article history:
Received 17 May 2018
Received in revised form 4 July 2018
Accepted 17 July 2018
Available online xxxx

ABSTRACT

Introduction: Cardiac tamponade is a severe complication of cardiac resynchronization therapy (CRT) implantations. We provide a contemporary large-scale study evaluating the incident trends, predictors and impact of cardiac tamponade in patients undergoing CRT.

Method: Data were obtained from the Nationwide Inpatient Sample (NIS) of 2007 through 2014. Trends in the annual rates of tamponades in CRT implantation were assessed using negative binomial regressions. Hierarchical mixed-effects logistic regression models were built to determine the independent predictors of tamponade in CRT implantation and 1:1 propensity-matched analysis performed to examine the impact of tamponade on outcomes.

Result: An estimated 310,704 CRT implantations were performed in the United States between 2007 and 2014, out of which 536 patients (0.17%) developed procedure-related cardiac tamponade. A significant increasing trend in the tamponade incidence was observed over the 8-year study period [1.65 per 10,000 CRT implantation in 2007 to 38.16 in 2014 ($p < 0.001$)]. After multivariable adjustment, female sex and coagulation disorder were found to be independently associated with higher odds of tamponade. Conversely, prior history of CABG procedure was associated with lower odds of tamponade. CRT complicated with tamponade had significantly increased in-hospital mortality, bleeding requiring transfusion, prolonged hospital stay and increased cost.

Conclusion: We found an increasing trend in the incidence of post CRT tamponade among hospitalized patients between 2007 and 2014. Female gender and coagulation disorder were associated with the development of tamponade among recipients of CRT. Risk stratification of patients who are undergoing CRT is crucial to improving outcome in CRT implantation.

1. Introduction

Cardiac resynchronization therapy (CRT) has been established as an effective alternative therapy for patients with advanced heart failure. However, its potential clinical benefits pivot on the proper implantation of a biventricular pacing system, to deliver effective resynchronization. This involves delicate cannulation of the thin wall coronary sinus and placement of a lead into one of the lateral branches, a technically challenging procedure with the potential for coronary sinus dissection and cardiac tamponade [1].

Cardiac tamponade is a severe complication of cardiac resynchronization therapy (CRT) implantations with significant morbidity and mortality. However, despite the elevated risk for coronary dissection and hence cardiac tamponade in CRT, the overall incidence and clinical outcomes of cardiac tamponade in CRT have not been extensively studied. While published event rates range from 0.1% to 0.8% for pacemaker leads [2, 3] and a recent study reported a prevalence of 0.28% coronary venous dissection in CRT [4], no large-scale study has evaluated the incidence of cardiac tamponade following CRT implantation. Also, no literature exists on the trend, predictors, and impact of cardiac tamponade on in-hospital outcomes.

Therefore, we provide a contemporary large-scale study evaluating the incident trend, predictors and impact of cardiac tamponade on hospital outcomes utilizing the largest all-payer, inpatient database in the United States - the National (Nationwide) Inpatient Sample (NIS).

* Corresponding author at: 360 Engle Street, Department of Internal Medicine, Englewood Hospital and Medical Center, Seton Hall University-Hackensack Meridian School of Medicine, Englewood, NJ, United States of America.
E-mail address: oluwoleadegbala@gmail.com (O. Adegbala).

https://doi.org/10.1016/j.ijcard.2018.07.084
0167-5273/

The relationship between key hospital and clinical variables and cardiac tamponade was examined, to identify independent predictors of tamponade and impact of tamponade on the outcomes of CRT implantation. Identification of patient characteristics associated with elevated risk of cardiac tamponade would help improve patient selection and area to be focused on in preventing this potentially catastrophic event.

2. Method section

2.1. Data source

Data were obtained from the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project–Nationwide Inpatient Sample (NIS) files between 2007 and 2014. The data was queried to identify patient demographics and risk profile for CRT recipients in the United States using the International Classification of Diseases-Ninth Revision-Clinical Modification (ICD-9-CM). The NIS contains deidentified patient-level data. Therefore the use of the NIS data is exempted from an Institutional Review Board approval. The database is robust and is a nationally representative survey of hospitalizations which was designed to annually compile a representative sample of hospital discharge records in the United States. The NIS includes data from approximately 1000 hospitals and is designed as a stratified, 20% representative sample of all nonfederal US hospitals. Criteria used for stratified sampling of hospitals into the NIS include hospital ownership, patient volume, teaching status, urban or rural location, and geographic region [5]. Weighting the patient-level observations in the NIS datasets to account for the complex sampling scheme provides estimates for the entire US population of hospitalized patients. Because the NIS was derived from state-mandated hospital discharge reports, it includes all claims from each selected hospital regardless of payer or insurance status.

2.2. Study design

The study population included all patients who underwent primary CRT implantation from 2007 to 2014. CRT implantation was identified by the presence of appropriate ICD-9 procedural codes in the individual discharge records. Patients who underwent implantation of CRT-P (biventricular pacemaker only, ICD-9-CM code 00.50) and CRT-D (biventricular pacemaker with defibrillator, ICD-9-CM code 00.51) devices were included in our study. We included only de novo implantation of devices and did not include generator changes, redo procedures, revisions, and related procedures. We also excluded stand-alone ICD placements.

The diagnostic code 423.3 was used to identify patients who developed cardiac tamponade during hospital admission in CRT implantation. These ICD-9-CM codes used were consistent during this study period, thus enabling cardiac tamponade incidence longitudinal trend analysis. The NIS discharge records were queried to identify demographics, including age, sex, race, insurance status, hospitalization outcomes such as bleeding requiring transfusion, and length of stay. Other variables included prior Percutaneous coronary intervention (PCI), prior coronary artery bypass graft (CABG), atrial fibrillation, prior cerebrovascular disease, dyslipidemia. These mentioned baseline characteristics were captured from the dataset with ICD-9-CM codes (Supplemental Table 1). To calculate the estimated cost of hospitalization the NIS data were merged with cost-to-charge ratios available from the Healthcare Cost and Utilization Project [6]. We estimated the cost of each inpatient stay by multiplying the total hospital charge with cost-to-charge ratios. Adjusted cost for each year was calculated regarding the 2017 cost, after adjusting for inflation according to the latest consumer price index (CPI) data released by US government on January 30, 2018 [7]. By doing this we standardized costs over the study period. The comorbidities associated with tamponade development were identified using Agency for Healthcare Research and Quality comorbidity measures. These comorbidity measures use ICD-9-CM diagnoses to identify different comorbidities on the discharge date. The severity of comorbidities was identified by using the Elixhauser comorbidity index [4]. Higher Index scores correspond to a greater burden of comorbid diseases.

2.3. Propensity score

We performed a comparative analysis between patients who underwent CRT complicated by tamponade and patients without tamponade. A propensity score (PS) matching model was developed to derive two matched groups for comparative outcomes analysis to account for potential confounding factors and reduce the effect of selection bias. The PS was calculated using multivariable logistic regression models derived from hospitals level, clinical, and demographic covariates, including the Elixhauser comorbidities. For the calculation of the PS, the dependent variable was the presence of tamponade. We performed matching on the PS implementing a greedy algorithm (gmatch macro) with no replacement to construct a balanced match of tamponade cases to patients without tamponade in a 1:1 ratio using a caliper of 0.1. We assessed the success of the match by performing Mc-Nemar's test for categorical variables and paired *t*-test for normally distributed continuous variables.

2.4. Statistical analysis

All the data extraction and analyses were done with Statistical Analysis System (SAS V.9.4, SAS Institute Inc., Cary, NC, US). We chose a p-value of <0.05, reported the effect sizes, 95% confidence intervals (CI), and p-values. For categorical variables, chi-square tests were used, and for non-normal distributed variables such as length of stay, Wilcoxon–Mann–Whitney test was used. Trends in the annual rates of tamponades in CRT implantation were assessed using negative binomial regressions with tamponade count as the dependent variable and calendar year as the key independent variable, with the number of CRT per year as an offset term.

Backward stepwise logistic regression models were built to determine the independent predictors of tamponade in the CRT implantation. The model included patient-level variables such as age, sex, and comorbidities as well as hospital-level variables such as hospital size (number of beds), hospital region, and teaching status. Choice of covariates for the multivariate analyses was based on the plausibility that they could be associated with cardiac tamponade. The c-indices of the models were acceptable, ranging from 0.77 to 0.80.

For the matched patient's clinical characteristics, we reported the mean and standard deviation (SD) for continuous variables and percentages for categorical variables. The baseline characteristics were computed with paired *t*-test for continuous variables with normal distribution and McNemar's test for categorical variables. We excluded all the missing variables from the analysis, and therefore, did a complete case analysis. Binary outcomes (in-patient mortality, bleeding requiring transfusion, acute kidney injury, discharge disposition) were modeled with binomial logistic regressions. Discrete numeric variables with an over-dispersed count distribution (length of stay) and continuous variables with a right-skewed spread (total hospital cost) were modeled with generalized linear model regressions, accounting for the matching, and with a negative binomial function and gamma function respectively. We reported odds ratio (OR) for our binary outcome, and mean ratios (MR) for the numeric outcomes.

As recommended by HCUP, analyses were performed in SAS with appropriate statements to account for the complex clustered sampling methodology [6].

3. Results

3.1. Baseline clinical characteristics

An estimated 310,704 CRT implantations were estimated in the United States between the years of 2007 and 2014. A total of 536 patients (0.17%) developed in-hospital cardiac tamponade during the study period. Patients' clinical characteristics and associated comorbidities are shown in Table 1. The mean age of patients who underwent CRT implantation was 70.27 (11.83) years. There was lower implantation in females (30.21%), and most implantations were done in the Medicare population (72.75%), urban-teaching (62.12%) and large bed-sized hospitals (72.02%). Atrial fibrillation, hypertension and diabetes mellitus were the most prevalent non-heart failure comorbidities.

Compared with CRT recipients who did not develop tamponade, patients with tamponade were more often women and had higher rates of coagulation disorders, higher Elixhauser comorbidity index and chronic deficiency anemia (Table 1). Conversely, Cardiac tamponade occurred less often among CRT recipients with a history of prior CABG procedure.

3.2. Trends in patients developing cardiac tamponade

As shown in Supplemental Table 2 and Fig. 1, a substantial increasing trend in the incidence of cardiac tamponade was observed over the 8-year study period [1.65 per 10,000 CRT implantation in 2007 to 38.16 in 2014 ($p < 0.001$)]. A similar trend was observed among patients who had CRT-P and CRT-D.

3.3. Predictors of cardiac tamponade

Table 2 demonstrates the independent factors associated with cardiac tamponade. After multivariable adjustment, female sex (adjusted odds ratio [aOR] 1.56; Confidence interval [CI] [1.003–2.418]) p-value 0.049) and coagulation disorder (aOR 5.39; CI [3.068–9.466] p-value < 0.0001) were found to be independently associated with greater odds of cardiac tamponade. These coagulation disorders encompass both inherited and acquired conditions predisposing to hemorrhage such as long-term anticoagulation and antiplatelet use, von-Willebrand disorder and coagulation factors deficiencies (Supplemental Table 4). Conversely, prior history of CABG procedure (aOR 0.049; CI [0.007–0.358] p-value 0.0029), and urban non-teaching hospitals (aOR 0.269; CI [0.103–0.699] p-value 0.0018), were associated

Please cite this article as: O. Adegbala, et al., Incidence and outcomes of cardiac tamponade in patients undergoing cardiac resynchronization therapy, Int J Cardiol (2018), https://doi.org/10.1016/j.ijcard.2018.07.084