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VA Hospital Cardiac Electronic Clinical Guideline Reminder Outcomes

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Abstract

U.S. Department of Veterans Affairs (VA) physicians receive guideline reminders to prescribe medications to patients recuperating from cardiac surgery. We examined whether these electronic clinical reminders were associated with a) medication fill rates and b) 6-month risk-adjusted survival after coronary artery bypass graft (CABG) surgery. This retrospective cohort study analyzed the national VA Pharmacy Benefits Management System and the Continuous Improvement in Cardiac Surgery Program data from 10/1/1999 to 9/30/2005.

Medication fill rates for a 6 month period prior to the active use of the electronic clinical reminder were compared with fill rates for a 12 month period after electronic reminder use. We found no significant difference in fill rates between the pre- and post-reminder periods.

An analysis of variance (ANOVA) model tested whether medication fill rates were affected by electronic reminders. Apparent differences in fill rates before and after implementing clinical reminders disappeared after controlling for multiple comparisons using false discovery rate; therefore data was pooled across years (antihypertensive medications (AH), p = 0.80 and lipid-lowering agent medication (LL), p = 0.30). Changes in fill rates for AH and LL were similar to each other (p = 0.37).

A Cox Proportional Hazard Regression model was used to determine the predictors of survival between the 6-month time period prior to the clinical reminder versus the 6-month time period after the reminder was actively used. The clinical reminders for both AHM and LLA were not significantly associated with survival (p = 0.45, hazard ratio = 2.2, confidence intervals 0.29-16).

These results do not support the use of electronic clinical reminders in this setting. Instead, these findings support questioning the utility of individual electronic record clinical reminders.

Keywords: Regression model; Analysis of variance; Lipid-lowering agent medication

Introduction

Approximately 16 million American adults suffer from Coronary Heart Disease (CHD); it is the number one single cause of death in the United States. Coronary Artery Bypass Graft (CABG), a procedure used to treat CHD, is a type of heart surgery which reroutes blood around clogged arteries to improve perfusion to the heart. Post-CABG patients are at an obvious risk of recurrence and thus need optimal secondary prevention after CABG in order to minimize future cardiac risk [1,2]. Post-CABG care often includes the use of antihypertensive (AH) and lipid lowering (LL) medications to prevent further cardiac health concerns. Through controlled clinical trials, these two classes of medications have been proven to be effective in terms of secondary prevention of negative cardiac outcomes after CABG [3-5]. Appropriate medication management of LL and AH therapy, through the use of clinical reminders, may impact the survival of post-CABG veterans.

The VA has developed a comprehensive Computerized Patient Record System (CPRS) that allows access to patient notes, lab values, medication orders and visit dates. Included in CPRS is a tool called Clinical Reminders, which is designed to prompt physicians to act on deficiencies in patient management. For example when a patient is suffering from hypertension, the computer prompts the physician to begin lifestyle counseling and therapeutic intervention. Electronic clinical reminders (ECR) for AH and LL agents are currently utilized at VA facilities through this tool (Table 1 for ECRs used in this study).

Clinical Guideline Reminders
Ischemic Heart Disease (IHD) Lipid Profile: The VHA/Department of Defense (DOD) Clinical Practice Guideline for Management of Dyslipidemia recommends that patients with Ischemic Heart Disease have a lipid profile/LDL every one to two years; and that patients taking lipid lowering medications have a lipid profile/LDL at least every year.
IHD Elevated LDL: The VHA/DOD Clinical Practice Guideline for Management of Dyslipidemia recommends an LDL goal of <120 mg/dl for patients with Ischemic Heart Disease; and the NCEP Adult Treatment Panel II recommends a more stringent goal of <100 mg/dl. Consider initiating or adjusting lipid lowering treatment.
Hypertension assessment for elevated blood pressure > 140/90: The most recent blood pressure was elevated. Satisfying this reminder requires addressing medication issues and/or education issues.

Table 1: Electronic Clinical Guideline Reminders Viewed by a Physician.

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The potential role of ECR is to improve guideline compliance with these medications, thus potentially improving quality of care and patient outcomes. However, to date there has been little formal evaluation of the effectiveness of ECR with regards to improving guideline compliance or influencing patient outcomes.

The goal of this project is to examine whether the ECR for AH and LL agents have impacted post-CABG medication fill rates and patient outcomes. Increasing medication fill rates and subsequently reducing mortality rates among the veteran population may result in longer-term veteran health benefits and VA-based cost savings if ECR are proven to be useful in improving secondary prevention compliance by enhancing the use rates for these medications in the future.

Materials and Methods

The Department of Veterans Affairs Continuous Improvement in Cardiac Surgery Program (CICSP) is a quality improvement program currently operating in over 40 VA cardiac surgery programs nationwide. CICSP has gathered data concerning patient risk factors, procedural details, and mortality information for all cardiac surgery procedures performed at VA facilities. Utilizing CICSP records, a de-identified data set from October 1999 to September 2005 of patients who underwent CABG was isolated for use in this study. The VA also keeps an electronic record of all medications filled at VA pharmacies known as the Pharmacy Benefits Management (PBM) System. Corresponding data was taken from the PBM system on the fill rates of LL and AH medications for patients in the data set extracted from the CICSP database. Medications classified as AH and LL agents are identified in Table 2. We combined data from these two databases to perform a retrospective cohort study was conducted to examine the association between ECR and LL and AH medication fill rates as well as six-month risk adjusted mortality rates in two specified groups, as described in Figure 1.

Specific aims

For post-CABG patients surviving to discharge, examine, for each of the two groups denoted in Figure 1:

1) The possible difference in the 6 month pre- and 12 month post-clinical guideline reminder fill rates for each medication that may be associated with active use of facility-based clinical guideline reminders.

2) The possible difference in the 6 month pre- and 6 month- post clinical guideline reminder risk-adjusted survival among patients receiving each medication that may be associated with active use of facility-based clinical guideline reminders.

Fill rates

ANOVA was used to assess the effect of clinical reminder on fill rates (Table 3). This method was chosen to allow for additional variables to be included and controlled for in the analysis. Hospital was used as the experimental unit. The independent variable of interest, the clinical reminders for AH and LL agents, was categorized by classifying the date of active date of use for each reminder and setting a time period of 6-months prior to this date as the baseline (pre-reminder) fill rate and 12-months after this date as the comparator (post-reminder) fill rate. The date of active use for the hypertension clinical reminder was used as Time 0 for the AH group. The date of active use for the LL clinical reminder was used as Time 0 for the LL group.

ACE (angiotensin-converting enzyme) inhibitors	**Angiotensin II Receptor (ARB) antagonists**
benazepril (Lotensin)	candesartan (Atacand)
captopril (Capoten, Nova-Captopril)	eprosartan (Tevetan, HTC)
enalapril,enalaprilat (Vasotec)	irbesartan (Avapro)
fosinopril (Monopril)	losartan (Cozaar)
lisinopril (Prinivil, Zestril)	telmisartan (Micardis)
moexipril (Univasc)	valsartan (Diovan)
perindopril (Aceon)	**Beta blockers (non-selective)**
quinapril (Accupril)	carteolol (Cartol)
ramipril (Altace)	carvedilol (Coreg)
trandolapril (Mavik)	labetolol (Nomodyne, Trandate)
Beta blockers (selective)	nadolol (Corgard)
acebutalol (Monitan, Sectral)	penbutolol (Levatol)
atenolol (Apo-atenolol, Tenomin)	pindolol (Novo-pindolol, Syn-pindolol, Visken)
betaxolol (Kerlone)	propanolol (Dentensol, Inderal, Novopranol)
bisoprolol (Zebeta)	timolol (Blocadren, Timoptic)
metoprolol (Betaloc, Lopressor, Toprol)	**Centrally-acting adrenergic agonists**
Calcium channel blockers	clonidine (Catapres, Duracion)
amlodipine (Norvasc)	methyldopa (Aldomet, Dopamet)
diltiazem (Cardizem, Dilacor-XR, Tiazac)	guanabenz
felodipine (Plendil, Renedil)	guanfacine
isradipine (DynaCirc)	**Peripherally-acting anti-adrenergics**
nicardipine (Cardene)	doxazosin (Cardura)
nifedipine (Adalat, Procardia, Apo-Nifed)	guanadrel (Hylorel)
nisoldipine (Sular)	prazosin (Minipres)
verapamil (Calan, Isoptin, Verelan)	terazosin (Hytrin)
Diuretics (thiazide)	**Vasodilators**
chlorothiazide (Diurigen, Diuril)	fenoldopam (Cortopam)
chlorathalidone (Hygroton, Thalitone, Uridon)	minoxidil (Loniten)
hydrochlorothiazide (Diaqua, Diachlor H, Esidrix, HydroDiuril, Hydromal, Oretic, Thiuretic, Urozide)	nitroprusside (Nitropress, Nipride)
indapamide (Lozide, Lozol)	**Antilipemic (lipid-lowering) drugs continued**
metalozone	gemfibrozil (Lopid)
Antilipemic (lipid-lowering) drugs	fluvastatin (Lescol)
atorvastatin (Lipitor)	lovastatin (Mevacor)
cholestyramine (LoCholest, Prevalite, Questran)	niacin (Endur-Acin, Nia-Bid)
cholesevalam	niacinamide (Niacor, Niaspin, Nicotinex)
cholestipol	pravastatin (Pravachol)
fenofibrate (Tricor)	simvastatin (Zocor)

Table 2: List of Antihypertensive and Lipid Lowering Agent Medications from the VA database that were analyzed to determine the fill rate.

Survival

Cox proportional hazard regression was performed to examine the association of clinical reminders between the six-month pre reminder time period and six-month post reminder time period (Table 4). This method was chosen because it is based on the timing of outcome which is critical since the ultimate goal in post-CABG patients is to extend life instead of curing disease. Survival analysis was used to evaluate the effect of clinical reminders and other risk factors on survival up to 1 year. The Cox regression also allows for the evaluation of multiple risk factors to determine the significance and magnitude of impact on the hazard.

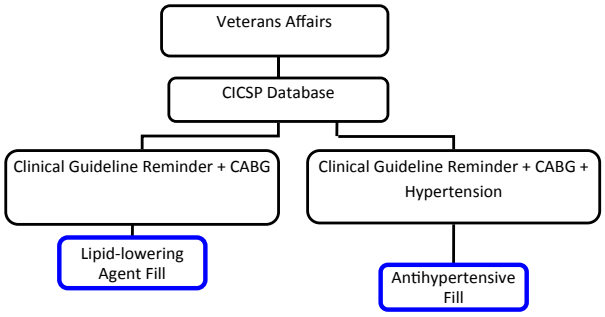

Figure 1: Patient Groups.

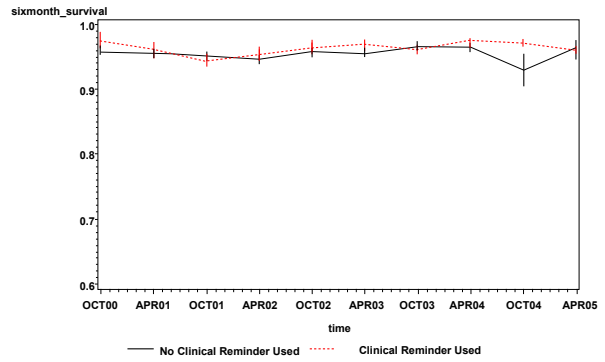

Figure 2: Six-month Survival in CABG only, Hypertension Patients with Antihypertensive Medication.

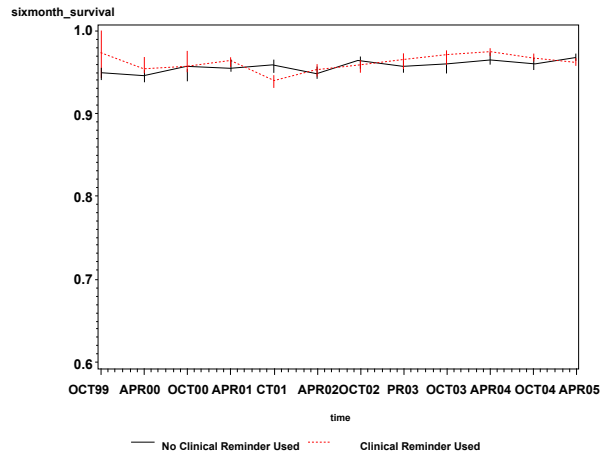

Figure 3: Six-month Survival in CABG only Patients with Lipid-lowering Agent Medication.

The survival analysis assessed 6 month risk adjusted survival 6 months prior to the clinical reminder and 6 months post the reminder. The following covariates were included in the model: time (before or after the clinical reminder), hospital, region (Northeast, Midwest, South, and West), 180-day mortality risk ratio, and smoking status. The rate of missing data for each covariate was checked prior to the analysis to ensure that a large number of patients were not being excluded due to a missing data point. This check confirmed that a significant number of patients were not being excluded based on missing covariate data. The model for this analysis was the time to death variable by the "alive" status variable and incorporating the covariates. The status variable was coded to classify whether a patient was alive or dead. The independent variable of interest, clinical reminders (coded as "time" – pre and post reminder) was included as a risk factor in the model to determine if it was statistically significant. The focus of this hypothesis was to determine if the clinical reminder impacted six-month risk adjusted survival.

Since the primary risk factor of interest was the clinical reminder, this model was rerun using both the 180-day mortality risk ratio and time (before or after the clinical reminder). This analysis demonstrated that the clinical reminder was not a statistically significant risk factor for survival. Therefore, to obtain the maximum number of patients in the analysis, the final model was run using only the 180-day mortality risk ratio. All observations reported are reflective of the final model.

This study was approved under an existing IRB approval with the Colorado Multiple Institutional Review Board. All data analyses were performed using the Statistical Analysis Software (SAS, Version 9.1).

Results

Fill rates

Results from the ANOVA model indicate that there was no statistically significant difference in fill rates for either medication during any year (apparent differences disappeared after controlling for multiple comparisons using false discovery rate); therefore data was pooled across years. Additionally, hospital was not significant in the analysis. The p values of 0.80 (AH) and 0.30 (LLA) represent the comparisons of the change in fill rate for each to zero. The p value of 0.37 assessed whether the changes in fill rates for AH and LLA were similar to each other. There was not a statistically significant difference in antihypertensive or lipid-lowering agent medication fill rates when comparing the change in fill rate (Post Reminder Fill Rate – Pre Reminder Fill Rate). When comparing the means, it is recognized that there was not a large increase in fill rates between the pre and post time period.

Survival

The predictors tested in each model (AH and LL) via Cox Proportional Hazard Regression included time (before or after the clinical reminder), hospital, region (Northeast, Midwest, South, West),

Response Variable (Dependent Variable)	Difference in AH and LLA medication fill rates from 6-months pre active use of the clinical reminder compared to 12-months post reminder
Independent Variable of Interest	Clinical Reminder for Hypertension and Lipid Lowering Agents
Cofactor Variables included in analysis	Hospital
Statistical Test Used	An analysis of variance model (Proc GLM)

Table 3: Fill Rate Analysis.

Six-month Survival Analysis	
Response Variable (Dependent Variable)	Six-month Risk adjusted survival: Variable coded as Time to Death (Calculated as Death date – Discharge Date)
Independent Variable of Interest	Clinical Reminder for Hypertension and Lipid Lowering Agents
Cofactor Variables included in analysis	Hospital, 180-day mortality risk, smoking status and region
Statistical Test Used	Cox proportional hazard regression

Table 4: Six-month Survival Analysis.

180-day mortality risk ratio, and smoking status. The time variable assessed the 6-month time period prior to active use of the reminder at each hospital and the 6-month time period following active use of the reminder. Summary tables of six-month survival for each group are below (Figures 2 and 3).

The total number of patients that met the criteria to be included in the LL group for the analysis was 6,819. In this group, 1 patient died in the 6-month time period prior to the reminder and 28 patients died in the 6 month time period post-reminder. Thus a total of 29 patients died in the LL group.

There were 6,823 patients that met the criteria to be included in the AH group. It is important to note that 51 patients died in the AH group.

The regression model for both groups indicated that the single most significant predictor of 6-month risk adjusted survival was the 180-day mortality risk ratio (Tables 5 and 6). All of the other predictors were excluded from each model since they did not contribute significantly to the explanatory power of the model. The hazard ratio for the AH group as well as the LL group was 1.09 which indicates that the hazard associated with 180 day mortality risk is 9%.

However, since the clinical reminder is the main focus of this project, the analysis was rerun with this variable since it was excluded during the stepwise selection of the final model. The clinical reminder was not statistically significant (p = 0.45, hazard ratio = 2.173, confidence intervals 0.294 -16.068). Since the clinical reminder was not statistically significant, it was excluded from the final model showing that the clinical reminder did not impact prescription fill rates enough to impact 6-month risk adjusted survival.

Discussion

Fill rates

There was no statistically significant difference in fill rate between the 6 month time period before the reminder when compared to 12 months after the reminder. Both LL and AH medications had high baseline fill rates with targeted clinical reminders. Since the baseline fill rate was so high on average across all VA hospitals for AH and LL agent medications, it left little room for improvement [6]. This suggests that the clinical reminders were not targeted at the right gaps in medication fill rates within the VA. A future study would be useful to examine a medication class that starts with low fill rates to determine if the reminder would have an impact since there would be significant room for change. However, it is possible that without the use of clinical reminders, the fill rates for these medications may have decreased over time. The clinical reminder may be associated with maintaining consistency in prescription fill rates.

Variable	Hazard Ratio	95% Hazard Ratio Confidence Limits	P-Value
Mortality_180	1.09	1.068-1.109	<.0001

[1]Excluded variables: time, hospital, region, copay, smoking status
[2]N = 7424

Table 5: Cox Proportional Hazard Regression Model Results for Survival in Post-CABG Patients with a Diagnosis of Hypertension and Receiving Antihypertensive Medication[1,2].

Variable	Hazard Ratio	95% Hazard Ratio Confidence Limits	P-Value
Mortality_180	1.09	1.059-1.113	<.0001

[1]Excluded variables: time, hospital, region, copay, smoking status
[2]N = 6823

Table 6: Cox Proportional Hazard Regression Model Results for Survival in Post-CABG Patients Receiving Lipid-lowering Agent Medication[1,2].

Most of the studies related to the use of clinical reminders have been done in an outpatient setting [7-12]. These studies did show an improvement in the use of clinical reminders, many of them for the use of preventive services. Additionally, one study conducted on inpatients did demonstrate significant improvements in the quality of patient care that was achieved as result of incorporating checklists and reminders into clinical pathways [13]. Therefore, there is evidence, although minimal, that clinical reminders can be effective for inpatient care.

Survival

There was no statistically significant difference in fill rate between the 6 month time period before the reminder when compared to 12 months after the reminder. Clinical guideline reminders for AH and LL agents did not demonstrate that prescription fill rates were impacted enough to demonstrate a change in 6-month risk adjusted survival. It is important to recognize that not many patients died during the 6-month pre reminder and 6 month post-reminder time period (51 patients died in the AH group and 29 patients died in the LL group); therefore the results of this study may be underestimated. Clinical reminders are not associated with an increase in survival rates secondary to increased medication fill rates.

The predictors tested for each group in this model included: time (before or after the clinical reminder), hospital, region (Northeast, Midwest, South, and West), 180-day mortality risk ratio, and smoking status. Since so few patients died during this time period, it was understandable that the clinical reminder was not significant (p = 0.45, hazard ratio = 2.173, confidence intervals 0.294 -16.068). Regarding the clinical reminder, it is important to notice the wide confidence interval in the results. The 180-day mortality risk ratio was the only significant variable in the model which is expected since it is the most valuable predictor of survival for each patient.

If clinical reminders increase prescription fill rates, and increased prescription fill rates lead to better medical outcomes, then it could be assumed that clinical reminders could result in higher survival rate. Studies have shown that poor adherence to medication regimens can contribute to higher mortality [14]. There is evidence that LL therapy reduces the risk of recurrent coronary events and improves survival in patients who have suffered a myocardial infarction [15,16]. While this study did not evaluate medication compliance, it does evaluate medication fill rates through prescriptions, which is the first step in the process.

The results of this hypothesis do not suggest that an association between clinical reminders and secondary clinical outcomes. Although, the main focus of clinical reminders in this study was fill rates, we wanted to evaluate if they impacted survival. It is essential to examine other potential outcomes that the clinical reminder may be affecting. It may not always be the primary outcome that has a significant change.

Limitations

There are several limitations to this project. This was a quasi-experimental study design that evaluated pre and post medication fill rates, not a true randomized controlled clinical trial. Perhaps the major limitation to this study is very high baseline prescription fill rates for the VA. The fill rate data for this study is based on data collected in

PBM system on whether a medication was filled at the VA pharmacy within 6 months of discharge. When compared to post-ECR fill rates, no significant difference was noted. However, it is certainly possible that the use of ECRs prevented a worsening of fill rates. In order to address this issue, a simultaneous control group without ECR intervention would have been useful. Similarly, another limitation is that the fill rate could be higher than calculated in this study if additional patients had their prescription filled outside the VA or obtained their prescription from a physician outside of the VA. However, obtaining prescriptions at the VA is often less expensive therefore patients most often do fill them through the VA pharmacy [17]. Finally, this analysis did not consider the effect of diet and lifestyle modifications that patients may have pursued post-CABG which may have confounded the reported results. There has also been a significant change in lipid testing over the last twenty years. From 1987 to 2007 there has been over a 15-fold increase in the amount of lipid tests ordered by providers [18]. This would cause a large increase in the number of high lipid levels detected and result in more reminders in the electronic medical record.

A recent study confirmed that prescription fill rates for post-CABG medications at VA hospitals were generally high and suggested compliance with guidelines for the prevention of cardiovascular events [6]. We also do not know if the patient actually took the medication as prescribed, despite successfully filling the prescription. Perhaps fill-rates are not adequate surrogates for clinical adherence. Some patients may use the VA for medication refills only while retaining a PCP in the community.

Conclusions

It is important to recognize that having a clinical reminder in place is a method of providing consistency of care across all patients. This study did not show an impact on fill rates or 6-month risk adjusted survival. However, the findings of this study cannot be generalized to the conclusion that reminders are not effective. It is also not feasible to implement a clinical reminder for every medication or disease that exists. It is critical not to overload the physicians that are using the reminders. This leads to additional questions that need additional research such as what diseases or medications should be targeted for clinical reminders, how long are clinical reminders effective after they are put into place and how many can be implemented before the physicians become overloaded. Additional future studies related to clinical reminders could take several different approaches. A researcher could obtain baseline data, then implement a specific clinical guideline reminder and follow it over time to determine how long it takes to adopt this new technology in daily practice and determine the impact of the reminder. Another study design would be to implement the clinical reminder at only a few hospitals or clinics and compare the changes to a hospital without the reminder. This would be more difficult since each hospital would possess a different population and specific hospital characteristics.

This study suggests that the use of electronic clinical guideline reminders does not improve medication fill rates or 6-month risk adjusted survival. Many barriers need to be overcome to obtain full benefit from clinical reminders. It takes time to implement new technology and to have physicians adapt to utilizing these new systems. It is essential that all clinical reminders be reviewed to ensure they are user friendly and useful to the physicians in their daily practice. Clinical reminders must fit into the normal workflow in order to be effective.

We recommend that electronic clinical guideline reminders should be evaluated on a case-by-case basis to determine if they may be useful in specific target populations.

Conflicts of Interest

The authors have no conflict of interest to declare. The opinions expressed in this article represent those of the authors and not of the government of the United States of America.

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