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Award Number: MIPR 3KD6LM3142

TITLE: Use of Beta-Blockers and Aspirin in Acute Coronary Syndromes by Patient Renal Function in the Military Healthcare Systems, National Capitol Area

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REPORT DATE: October 2005

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
01-10-2005	Final	15 Jul 03 – 30 Sep 05

4. TITLE AND SUBTITLE
Use of Beta-Blockers and Aspirin in Acute Coronary Syndromes by Patient Renal Function in the Military Healthcare Systems, National Capitol Area

5a. CONTRACT NUMBER

5b. GRANT NUMBER
MIPR 3KD6LM3142

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Walter Reed Army Medical Center
Washington, DC 20307-5001

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Whether the previously reported underutilization of standard-of-care medications in the management of acute myocardial infarction (AMI) persists in more recent years or differs by ward of admission has not been reported. We performed a cross-sectional study of patients admitted with initial episodes of AMI to a Department of Defense (DOD) hospital system from 2001 through 2004. Use of beta-blockers (BB) and aspirin (ASA) at the time of discharge after AMI was assessed according to serum creatinine level, stratified by admission to the coronary care unit (CCU) vs. other wards. Adjusted odds ratios for discharge BB and ASA were calculated by logistic regression. Among 453 patients, overall use of BB was 84.5% and ASA 83.7%, both significantly higher after CCU admission than admission to other wards (90.1% ASA and 91.0% BB use; P <0.001 and P <0.001). Among CCU patients with the highest quartile of serum creatinine (≥1.6 mg/dl), BB use was 93.3% and ASA use 87.3%. Among non-CCU patients in the highest quartile of serum creatinine, BB use was 68.5% and ASA use was 71.2%. In logistic regression, the log-transformed serum creatinine was significantly associated with BB and ASA use only among non-CCU patients (p=0.035). Contraindications to ASA, but not BB use, were frequent among patients admitted to other wards and with serum creatinine ≥2.5 mg/dl. In the DOD health system in recent years, admission to the CCU for AMI was not associated with significant underutilization of BB and ASA among patients with renal insufficiency.

15. SUBJECT TERMS
Beta blockers, Aspirin, myocardial infarction, creatinine, kidney

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	29	19b. TELEPHONE NUMBER *(include area code)*

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Use of Beta-blockers and Aspirin after Myocardial Infarction by Patient Renal Function in the Department of Defense Healthcare System: Exploring Barriers to Quality

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Word count: 3486

Disclaimer: the opinions expressed are those of the authors and do not constitute an endorsement by the Department of Defense

Abstract

Whether the previously reported underutilization of standard-of-care medications in the management of acute myocardial infarction (AMI) persists in more recent years or differs by ward of admission has not been reported. We performed a cross-sectional study of patients admitted with initial episodes of AMI to a Department of Defense (DOD) hospital system from 2001 through 2004. Use of beta-blockers (BB) and aspirin (ASA) at the time of discharge after AMI was assessed according to serum creatinine level, stratified by admission to the coronary care unit (CCU) vs. other wards. Adjusted odds ratios for discharge BB and ASA were calculated by logistic regression. Among 453 patients, overall use of BB was 84.5% and ASA 83.7%, both significantly higher after CCU admission than admission to other wards (90.1% ASA and 91.0% BB use; P <0.001 and P <0.001). Among CCU patients with the highest quartile of serum creatinine (≥1.6 mg/dl), BB use was 93.3% and ASA use 87.3%. Among non-CCU patients in the highest quartile of serum creatinine, BB use was 68.5% and ASA use was 71.2%. In logistic regression, the log-transformed serum creatinine was significantly associated with BB and ASA use only among non-CCU patients (p=0.035). Contraindications to ASA, but not BB use, were frequent among patients admitted to other wards and with serum creatinine ≥2.5 mg/dl. In the DOD health system in recent years, admission to the CCU for AMI was not associated with significant underutilization of BB and ASA among patients with renal insufficiency.

Introduction

It is well known that patients with abnormal renal function, whether mild or among patients receiving dialysis or transplantation, are at greatly increased risk of heart disease and heart disease-related mortality compared to the general population.[i,ii,iii,iv] Whether this increased risk is due to standard risk factors for heart disease such as diabetes,[v] the most common cause of chronic kidney disease in the United States,[vi] or factors unique to renal insufficiency is currently controversial. [vii]

Despite their high risk, standard therapies for treatment and prevention of coronary heart disease appear to be underutilized among patients with renal insufficiency. Specifically, under-use of standard of care medications after MI has been reported among patients with chronic kidney disease and dialysis-dependence studied as recently as the year 2000 [viii,ix,x,xi,xii], despite strong beneficial associations in this setting. So far, no study has identified either a clear explanation for such underutilization, or how such underutilization can be improved.

To assess whether such practices have continued in more recent years and/or vary with location of care within an acute care hospital, we studied a cohort of patients from the Department of Defense healthcare system. Since all prescribed medications are provided without cost in this system, financial disparities and incentives should be minimized in studies of utilization patterns among its members. Our hypothesis was that underutilization of standard of care medications would not differ significantly by level of renal function, after accounting for site of care.

Methods

Study Sample: We used the Integrated Clinical Database (ICDB™) database (ICDBNCA Oracle database), a read-only image of the Composite Health Care System (I-CHCS™) of the consolidated national capitol area (NCA), to identify adults aged 18 years or older hospitalized from 1 Jan 2001-27 April 2004 with acute MI. We collaborated with the ICDB team (Telemedicine Directorate) in the extraction of data from the ICDB, including retrieval of inpatient information from the Clinical Information System (CIS™, Datacomp). All patient identifying information was replaced by unique patient identifiers (UPI) that cannot be traced back to identify individual patients. UPI was removed after extraction from the ICDB and stored in an Excel™, Access™, or SPSS™ format. Telemedicine staff were trained on the use of Oracle to extract information from the ICDB and from CIS to obtain the needed information in a confidential fashion. Unique patient identifiers was removed and replaced with anonymous study codes after creation of all necessary variables for analysis. Information in full text fields that contained patient identifying information were also removed. This protocol was approved by the Walter Reed Human Use Committee as an exempt review protocol.

Outcomes: The primary outcomes were beta blockers and aspirin use at or within one week of the date of discharge for acute MI defined as a hospitalization with a discharge diagnosis for active or initial episode of care for acute myocardial infarction, International Classification of Diseases, 9th Edition (ICD-9) code 410.x, excluding codes for "subsequent episodes of care". Qualifying medication use comprised both new prescriptions and continuation of previous prescriptions.

Covariates: The primary dependent variable was renal function, defined as the serum creatinine level. Although K/DOQI has defined chronic kidney disease in stages as calculated from the

modified MDRD formula,[xiii,xiv] this formula requires identification of black race, which was not accurately tracked in ICDB. The Cockcroft-Gault creatinine clearance requires identification of weight which was not routinely available in the database. Serum creatinine was also categorized according to previous reports such as Shlipak et al[x] for purposes of comparison. Other variables included age, race (white vs. other), diabetes (defined as an ICD9 diagnosis or use of insulin or hypoglycemic medications), marital status, military rank as a surrogate for socioeconomic status (officer vs. enlisted), and primary ward of admission (primarily coronary care unit vs. others).

For patients with serum creatinine levels ≥2.5 mg/dl, separate chart audit was performed (N=66) to verify diagnosis of AMI, serum creatinine level, death during admission, discharge medication use of aspirin and/or beta blockers, and contraindications to or complications precluding the use of aspirin or beta blockers. Because this abstraction was not performed for all patients in the study, the impact of contraindications/complications is presented for descriptive purposes only, and was not subjected to formal statistical analysis.

Data extraction: Oracle™ was used for extraction of data from the ICDB, and Microsoft Excel™ or Access™ format. DBMS Copy™ was used for more sophisticated handling of dates, merging files if needed, and elimination of duplicate entries. All patient identifying information was removed upon entry of data from patient record sources into spreadsheet form, and replaced with anonymous unique patient identifying codes that cannot be traced back into the original records, similar to the system used by the United States Renal Data System (www.usrds.org).

Statistical analysis: SPSS™ v 12.0 was used for statistical analysis. In univariate analysis, Chi square testing was used for categorical variables (including tests for linear trend of categories of renal function) and Student's t-test was used for continuous variables with a normal distribution. Alpha values was set at 0.05 (two-tailed). Alternate tests were used for special circumstances

(Fisher exact test for categorical variables with violations of Cochran's assumptions, the Wilcoxon rank sum test or Mann-Whitney test as alternatives for the t-test for continuous variables without Gaussian distributions). Multiple logistic regression analysis was performed separately to assess factors independently associated with beta blocker and aspirin use, respectively. Variables that were associated with a p-value of <0.1 or were otherwise suspected to be associated with beta blocker or aspirin use, respectively, were included in the logistic regression model for multivariate analysis. Because serum creatinine values were skewed to the right, these values were logarithmically transformed prior to entry into the logistic model. Age was highly skewed to the left, and was transformed as the square of age. Variables that were significant with a p-value of <0.05 after multivariate analysis were considered to be independently associated with beta blocker and aspirin use. The predictive accuracy of the model was assessed using the concordance c index, which is equivalent to the area under the receiver operator curve (ROC) curve for the model (1.0 indicating perfect agreement, 0.5 indicating random agreement). Model fit was assessed using Hosmer-Lemeshow diagnostics.

Sample Size: The analysis was retrospective, and therefore sample size analysis is not entirely appropriate. However, as a guide to determine how many patients was sufficient to avoid type II error, analysis was performed to determine sample sizes needed for a power of 80% and an alpha of 0.05 using the same proportions reported previously, using a continuity correction to the usual sample-size formula based on the normal approximation to the binomial distribution.[xv] In order to avoid type II error, and based on previous reports, we estimated we would need the following patients for this analysis:

Aspirin use: Shlipak data[x]: 112 patients with Scr 2.5-3.9 mg/dl (used in 58%)

Beta blocker use: Shlipak data: 81 patients with Scr 2.5-3.9 mg/dl (used in 27%).

Results

476 patients were admitted for initial episodes of acute myocardial infarction during the study period. Of these, 23 (4.8%) died during the hospitalization and thus were not eligible to receive discharge medications (by quartile of serum creatinine, 4.9% died during admission in the lowest quartile compared to 11.6% in the highest quartile, $p<0.001$ by Chi Square). Excluding patients who died during admission thus left 453 patients available for analysis. Overall, 84.5% of patients were discharged with beta-blockers and 83.7% were discharged with aspirin. Of patients prescribed beta-blockers, 90.1% were also prescribed aspirin, and of those prescribed aspirin, 91% were also prescribed beta blockers. Demographics of the study population are shown in Table 1, which demonstrate an elderly, predominantly white male population. In univariate analysis, the factor most significantly associated with use of aspirin or beta blocker use overall was admission to the coronary care unit (CCU), as opposed to other admitting locations. Among patients admitted to the CCU, aspirin use was 89.8%, compared to 77.1% in patients admitted to other wards ($p<0.001$ by chi square). Among patients admitted to the CCU, beta-blocker use was 91.9% compared to 76.6% in other wards (($p<0.001$ by chi square). Insulin use was of borderline significance for associated aspirin use, 88.9% vs. 79.7%, $p=0.055$ by Chi Square, while diabetes was not. Insulin use was not significantly associated with beta blocker use. Patient age was not significantly associated with beta blocker use (71.1 ± 15.1 years for those with beta blocker use vs. 68.4 ± 13.1 years for those without beta blocker use, $p=0.095$ by Student's t-test) or with aspirin use (70.0 ± 14.3 years for those with aspirin use vs. 68.6 ± 13.3 for those without aspirin use, $p=0.37$ by Student's t-test). Use of beta blockers and aspirin also did not differ by year of admission (2003 and later vs. earlier), even when stratified by level of kidney function.

Because primary admission to the CCU was the factor most significantly associated with aspirin and beta blocker use, and some studies have limited analysis exclusively to patients

admitted to the CCU, Table 2 shows the association of beta blocker and aspirin use with level of renal function stratified by admission to CCU vs. other wards. The linear trend of association of beta blocker and aspirin use with quartile of kidney function was not statistically significant. However, when stratified by serum creatinine level of ≥2.5 mg/dl vs. below, aspirin use was significantly less common among patients with a serum creatinine level of ≥2.5 mg/dl who were admitted to a ward other than the CCU (p=0.03 by Chi Square).

Table 3 shows results of logistic regression analysis of factors associated with aspirin and beta blockers, using two models: one excluding CCU admission as a variable, and the other including it. In the first model, the natural logarithm of serum creatinine was significantly associated with aspirin use, as were active duty status and insulin use, while the transformed creatinine was not significantly associated with beta blocker use. In the model including admission to the CCU, serum creatinine was not significantly associated with either aspirin or beta blocker use. CCU admission was not significant as an interaction term with serum creatinine level in either model. However, in a model limited to patients who were not admitted to the CCU, the logarithm of serum creatinine was significantly associated with aspirin use (adjusted odds ratio, 0.61, 95% CI, 0.38-0.98), but not with beta blocker use (adjusted odds ration, 0.79, 95% CI, 0.48-1.29).

Independent chart audits were performed looking at the 66 patients who had serum creatinine levels of 2.5 mg/dl or higher, to confirm diagnosis of AMI, level of serum creatinine, discharge medication use, and deaths during admission. Audit confirmed serum creatinine level, the diagnosis of myocardial infarction and use of beta blockers and aspirin at discharge as reported through the CHCS system in all patients, and deaths. Four patients had gastrointestinal bleeds (one of these patients was discharged to hospice), one patient had uncontrolled hemorrhage attributed to use of heparin, one patient was treated with coumadin for atrial fibrillation, one patient refused treatment, and one patient had an exacerbation of chronic

obstructive lung disease and was therefore not treated with beta blockers. In only one case where aspirin was not prescribed was there not a legitimate contraindication to the use of aspirin (coumadin use was considered a contraindication to aspirin use during the time of the study), and in two cases where beta blockers were not prescribed. Six of the seven legitimate contraindications to aspirin use occurred among patients admitted for AMI to wards other than the CCU. The only documented contraindication to use of beta blockers also occurred in a patient not admitted to the CCU. In Tables 2 and 3, exclusion of patients with contraindications to aspirin and beta-blocker use, respectively, resulted in attenuation of the differences in medication use associated with differing levels of serum creatinine, but not elimination of this difference. In logistic regression, in the model which excluded cases where aspirin was contraindicated, the association of serum creatinine with aspirin was not statistically significant.

Discussion

In a Department of Defense health system, we found that the serum creatinine level was not independently associated with the discharge use of beta blockers or aspirin after hospitalization for initial myocardial infarction, except in analysis restricted to patients who were admitted to wards other than the coronary care unit. In fact, in the present study, the overall use of aspirin and beta blockers at discharge for myocardial infarction among patients with impaired renal function was substantially higher than in previous reports[12-14,xvi].

Because of differences in study design, head-to-head comparison of medication use is not possible between studies. However, in Table 2 of the present study we used serum creatinine categories similar to that of Shlipak et al[10]. The study of Shlipak et al assessed Medicare patients hospitalized for myocardial infarction in 1994 and 1995, although this analysis was not restricted to CCU patients and did not distinguish by admission ward. In that study, aspirin use was 83% in patients with serum creatinine <1.5 mg/dl, 73% in patients with serum creatinine 1.5-2.4 mg/dl, and 64% in patients with serum creatinine 2.5-3.9 mg/dl. Additionally, in that study, corresponding figures for "ideal" candidates for beta blocker use were 57%, 46%, and 40%, respectively. In Table 2 from the present study, among patients admitted to the CCU, use of beta blockers was higher even than for ideal candidates in the Shlipak study, while among patients admitted outside the CCU usage of beta blockers was at least 20% higher than in the Shlipak study. The differential was much less distinct for aspirin use among patients not admitted to the CCU. In fact, among patients not admitted to the CCU with a serum creatinine of <1.5 mg/dl, usage of aspirin was actually lower (80.3%) than in the study of Shlipak et al (83%), and almost identical at other levels of kidney function (75.6% vs 73%, and 68.2% vs. 64%). Among patients admitted to the CCU, however, usage of aspirin was substantially higher at every level of creatinine than in the study of Shlipak et al.

In the report of Wright et al[9], which was limited to patients admitted to the CCU in a single center from 1988-2000, the use of beta blockers among patients with normal renal function (which they defined as a Cockcroft-Gault creatinine clearance of >75 ml/min) was 85%, and aspirin use was 89%, while for patients with moderate renal insufficiency (creatinine clearance of ≥35 ml/min but <50 ml/min) beta blocker use was 66% and aspirin use was 73%; all differences were statistically significant. Due to data collection limitations we could not directly compare levels of Cockcroft-Gault creatinine clearance between that and the present study. However, in the present study among patients admitted to the CCU with serum creatinine 2.5-3.9 mg/dl, both aspirin and beta-blocker use were considerably higher (90.9% vs. 66%) higher than in the study of Wright et al for patients with a Cockcroft-Gault creatinine clearance of >35 but <50 cc/min. Even so, an appreciable decrease in beta-blocker use among patients admitted to the CCU was not noted consistently at any level of serum creatinine in the DOD system. Among CCU patients in the present study, aspirin use was actually highest among the patients with the highest serum creatinine levels. The study of Wright et al was limited to patients admitted to the CCU, and remarkably, even in this setting, and even after rigorous chart review to exclude patients with accepted contraindications to use of standard therapy, a disparity of beta blocker and aspirin use was noted among patients with renal insufficiency. The authors found that contraindications to therapy were more common among patients with any degree of dysfunction, and the high frequency of medical complications among our cohort of patients with high serum creatinine levels is consistent with this observation. However, the authors did not assess whether this practice changed during the more recent years of their study (as it covered the period from 1988-2000). Thus, it is possible the results of the present study would be comparable with the more recent years of that study. The study of Shlipak et al assessed Medicare patients with a diagnosis of acute myocardial infarction, and thus not all patients were admitted to the CCU.

Aspirin use among patients with renal insufficiency had earlier been discouraged because of concerns of bleeding diathesis among these patients[xvii]. The present study verified a high rate of gastrointestinal bleeding noted among patients with the highest levels of serum creatinine, consistent with the high risk of gastrointestinal bleeding noted among the end stage renal disease population. Accounting for legitimate contraindications to aspirin use in the present study attenuated but did not eliminate disparity in aspirin use among patients with higher levels of serum creatinine. The Physicians' Desk reference still advises against the use of aspirin in patients with creatinine clearance of <10 ml/min, even though the American Diabetes Association practice guidelines recommend the use of aspirin as primary prevention in all patients with diabetes (who account for nearly 50% of all long-term dialysis patients in the US) with risk factors[xviii], without specific mention of kidney function. Thus, patients with renal insufficiency present a vexing dilemma: on one hand they have perhaps the greatest need for aspirin in a setting of AMI, but on the other hand they also appear to have a high rate of contraindications to aspirin use.

The underutilization of beta blockers in patients with renal insufficiency is more difficult to explain, since lipid soluble beta blockers do not need to be dose adjusted even in severe renal disease, and can easily exchanged for water soluble beta blockers. Patients with renal insufficiency are more likely to have diabetes than patients with normal renal function, and in the past beta blockers have been avoided in diabetes for fear of masking signs of hypoglycemia. However, in more recent years beta blockers have not been withheld from diabetics because it is appreciated that diabetics have a high risk of heart disease. Only one legitimate contraindication to beta-blocker use was identified in the present study, and did not affect results of analysis.

The significant association of discharge aspirin and beta-blocker use with admission to the CCU vs. other wards highlights the importance of accounting for the primary site of admission for patients with AMI. Post-operative myocardial infarction, especially after

abdominal surgery, might be considered higher risk for the use of aspirin, although most cardiologists would consider the bleeding risk associated with aspirin minimal. Beta blockers are now routinely prescribed perioperatively for high-risk patients[xix], and in current management would only be avoided in a setting of fulminate heart failure[xx]. Clearly CCU's are focused on the management of myocardial infarction, by definition, and such focus may follow the patient past transfer to other wards (after admission to the CCU for confirmed myocardial infarction, patients are almost always transferred to the cardiology ward or step-down unit; thus initial admission to the CCU may also be a marker for closer and more focused cardiology follow-up in certain healthcare systems). In this setting, discharge planning incorporates established protocols and safeguards that patients who experience myocardial infarctions on other wards may not have access to, and such practices may need to be extended globally to the entire health system.

The current study is limited by its cross-sectional design, which can only determine associations, not establish causation. Despite chart review and available demographics, we cannot ensure that the patients admitted to the CCU are truly comparable to those admitted to other wards, and thus the circumstances attending their diagnosis and management might also differ systematically in ways unmeasured by the present study. The present study did not assess outcomes such as long-term mortality or other complications after myocardial infarction and whether these differed by renal function, as described in many of the previously cited references. The MDRD formula[xiii] and Cockcroft-Gault formula[xxi] were not used due to limitations of the data collection as previously stated. However, while the study of Wright et al used the Cockcroft-Gault formula, limitations of other large databases led other investigators such as Shlipak et al to rely on serum creatinine determinations, as we did in the present study.

In summary, the present study found that in a contemporary cohort of patients admitted for acute myocardial infarction to a Coronary Care Unit in the Department of Defense health system, beta blockers and aspirin were not significantly underutilized in association with renal insufficiency. In contrast, patients who experienced myocardial infarction in other settings did have underutilization of aspirin associated with renal insufficiency, although this disparity was largely, but not entirely, accounted for by a

high rate of legitimate contraindications to aspirin use; these contraindications would not have been apparent by relying on coding alone. Patients with advanced CKD truly are high-risk for complications from standard of care therapy, and while as a group they benefit from the use of such medications, careful patient selection is necessary to avoid drug related adverse events.

Acknowledgements and funding:
The authors would like to acknowledge and appreciate the time and assistance of the entire North Atlantic Regional Medical Command Telemedicine Directorate, Walter Reed AMC, Washington, DC, and the Telemedicine and Technology Research Center (TATRC), Ft. Detrick, MD for their help in planning and executing this project. This project received $88,000.00 in funding from a Program 6 Grant provided by TATRC (www.tatrc.org).

Table 1

Patient Demographics of the study population

Age (years)	68.6±13.6, range 29-96
Male (vs. female)	309 (68.2)
Caucasian (vs. all other races)	318 (70.2)
Married (vs. single, widowed or divorced)	347 (76.6)
Active Duty (vs. retired or dependent)	34 (7.5)
Officer (vs. enlisted or warrant)	107 (23.6)
Diabetes (vs. nondiabetic)	163 (36.0)
Insulin use (vs. all other medications)	81 (17)
Serum creatinine (mg/dl)	1.58 (1.37), range 0.4-11.5
Date of Admission (range)	1/9/2001-3/26/2004
Coronary Care Unit Admission	235 (51.9)

Data presented as mean ± standard deviation for continuous variables, or N (%) for categorical variables.

Table 2

Use of Aspirin and Beta Blockers by serum creatinine level, stratified by admission to CCU or other wards

	CCU Admission		Non CCU Admission	
	Beta Blockers	**Aspirin**	**Beta Blockers**	**Aspirin**
Quartiles of serum creatinine, mg/dl				
1: ≤0.9	61 (92.4)	62 (91.2)	40 (80.0)	40 (80)
2: >0.9-1.1	55 (90.2)	51 (82.3)	30 (71.4)	34 (81.0)
3: ≥1.2-1.5	58 (92.1)	48 (96)	47 (88.7)	42 (79.2)
4: ≥1.6	42 (93.3)	55 (87.3)	50 (68.5)	52 (71.2)
Serum creatinine ≥5.0	3 (100%)	4 (100%)	5 (55.6)	4 (44.4)**
Serum creatinine ≥5.0 excl contraindications¥	3 (100%)	4 (100%)	5 (55.6)	3 (50)
Categories of Serum creatinine per Shlipak et al[10]				
Serum creatinine <1.5	163 (92.1)	160 (90.4)	109 (79.6)	110 (80.3)
Serum creatinine 1.5-2.4	35 (89.7)	33 (84.6)	34 (75.6)	34 (75.6)
Serum creatinine 2.5-3.9	10 (90.9)	10 (90.9)	14 (63.6)	15 (68.2)
Serum creatinine 2.5-3.9 excl contraindications¥	10 (90.9)	10 (90.9)	14 (66.7)	14 (73.7)
Serum creatinine ≥4.0	8 (100)	8 (100)	10 (71.4)	9 (64.3)
Serum creatinine ≥4.0 excl contraindications¥	8 (100)	8 (100)	10 (71.4)	8 (72.7)

CCU=coronary care unit

Data presented as N (%), the number and % of patients in each category of serum creatinine level who received beta blocker or aspirin, respectively, at discharge, stratified by admission to the CCU vs. other wards.

*=p=0.03 vs. Aspirin use in non CCU patients with serum creatinine <2.5

**=p=0.04 vs. Aspirin use in non CCU patients with serum creatinine <5.0

Contraindications for aspirin included gastrointestinal bleeding, hemorrhage due to systemic heparinization, refusal of therapy, or terminal illness (N=7). Contraindications for beta blockers included exacerbation of chronic obstructive airways disease (N=1).

¥ Extraction of contraindications to aspirin or beta blocker therapy was performed only for patients with serum creatinine level $\geq$2.5 mg/dl, and thus this information is presented for descriptive purposes only, not subject to statistical analysis.

Table 3 Logistic Regression of Factors associated with use of beta blockers and aspirin

	Adjusted Odds Ratio for beta blocker use (95% CI)	**Adjusted Odds Ratio for aspirin use (95% CI)**
Model 1: excluding CCU admission		
Natural logarithm of serum creatinine (per log mg/dl increase)	0.71 (0.42-1.19)	0.57 (0.34-0.96)*
Natural logarithm of serum creatinine (per log mg/dl increase) excluding contraindications¥	NA	0.63 (0.35-1.13)
Insulin use	2.40 (0.96-6.00)	2.78 (1.05-7.36)*
Model 2: including CCU admission		
CCU	3.29 (1.86-5.84)*	2.53 (1.47-4.34)*
Natural logarithm of serum creatinine (per log mg/dl increase)	0.76 (0.48-1.22)	0.67 (0.43-1.05)
Natural logarithm of serum creatinine (per log mg/dl increase) excluding contraindications¥	NA	0.75 (0.45-1.24)

*=<0.05 in logistic regression

Predictor variables in each model included age, race, gender, rank, diabetes, insulin use, and natural log of serum creatinine. Model 1 excluded patients admitted to the CCU. Model two also included admission to the CCU as a predictor variable.

Contraindications to aspirin use as in Table 2. Values for contraindications to beta-blocker use are not given since only one contraindication was documented.

¥Extraction of contraindications to aspirin or beta blocker therapy was performed only for patients with serum creatinine level ≥2.5 mg/dl, and thus this information is presented for descriptive purposes only, not subject to rigorous statistical analysis.

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