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The interaction between pre-admission β-blocker therapy, the Revised Cardiac Risk Index, and mortality in geriatric hip fracture patients

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BACKGROUND: An association between β-blocker (BB) therapy and a reduced risk of major cardiac events and mortality in patients undergoing surgery for hip fractures has previously been demonstrated. Furthermore, a relationship between an increased Revised Cardiac Risk Index (RCRI) score and a higher risk of postoperative mortality has also been detected. The purpose of the current study was to investigate the interaction between BB therapy and RCRI in relation to 30-day postoperative mortality in geriatric patients after hip fracture surgery.

METHODS: All patients older than 65 years who underwent primary emergency hip fracture surgery in Sweden between January 1, 2008, and December 31, 2017, except for pathological fractures, were included in this retrospective cohort study. Patients were divided into cohorts based on their RCRI score (RCRI 1, 2, 3, and ≥4) and whether they had ongoing BB therapy at the time of admission. A Poisson regression model with robust standard errors of variance was used, while adjusting for confounders, to evaluate the association between BB therapy, RCRI, and 30-day mortality.

RESULTS: A total of 126,934 cases met the study inclusion criteria. β-Blocker therapy was associated with a 65% decrease in the risk of 30-day postoperative mortality in the whole study population (adjusted incidence rate ratio [95% confidence interval], 0.35 [0.32–0.38]; $p < 0.001$). The use of BB also resulted in a significant reduction in 30-day postoperative mortality within all RCRI cohorts. However, the most pronounced effect of BB therapy was seen in patients with an RCRI score greater than 0.

CONCLUSION: β-Blocker therapy is associated with a reduction in 30-day postoperative mortality, irrespective of RCRI score. Furthermore, patients with an elevated cardiac risk appear to have a greater benefit of BB therapy. (*J Trauma Acute Care Surg.* 2022;92: 49–56. Copyright © 2021 The Author(s). Published by the American Association for the Surgery of Trauma.)

LEVEL OF EVIDENCE: Therapeutic/care management, level II

KEY WORDS: β-Blocker therapy; hip fracture; Revised Cardiac Risk Index; mortality.

The incidence of hip fractures is expected to increase over the coming years as a result of the rapidly aging global population.[1–4] The mortality rate among hip fracture patients is high and places a heavy burden on the healthcare system and society.[5,6] Hip fracture patients generally suffer from several comorbidities with the primary cause of mortality being cardiovascular events.[5,7–10] Several studies have demonstrated that β-blockers (BBs) are able to reduce the risk of major cardiac events and mortality in patients undergoing noncardiac surgery.[9,11–15] Recent published studies have also demonstrated an association between BB usage and reduced short-term postoperative mortality in traumatic hip fracture patients.[9,13]

The protective effects of BBs are mainly seen in patients with preexisting cardiac risk factors.[16] The Revised Cardiac Risk Index (RCRI), initially developed by Lee et al.,[17] has been used to evaluate the 30-day risk of major cardiac events and all-cause mortality in the postoperative period.[18] The relationship between a high RCRI score and increased postoperative mortality has been demonstrated in several studies on patients undergoing noncardiac surgery.[18–20] A recent study, including patients only operated on for traumatic hip fractures, also demonstrated an association between an increased RCRI score and a higher risk of short-term postoperative mortality.[21] The aim of this study was to investigate the interaction between preoperative BB therapy and the RCRI score in relation to 30-day postoperative mortality in geriatric patients after hip fracture surgery. The hypothesis was that patients with higher RCRI scores will have a greater benefit of BB therapy, in terms of reduced postoperative mortality.

PATIENTS AND METHODS

This study complies with the principles of the Declaration of Helsinki and the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[22] Ethical approval was obtained from the Swedish Ethical Review Authority

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(reference 2021-01744). The cohort was retrieved from the prospectively collected Swedish National Quality Registry for Hip Fractures, Rikshöft.[23] Cases were considered for inclusion if the patient was older than 65 years and underwent primary emergency hip fracture surgery in Sweden between January 1, 2008, and December 31, 2017. Conservatively treated and pathological hip fractures were excluded from the original data retrieval. The data from Rikshöft were used to determine the date of hospital admission, age, sex, fracture type, American Society of Anesthesiologist (ASA) classification, type of surgery, date of surgery, and hospital discharge date. This was cross-referenced with the Swedish National Board of Health and Welfare Patient, Cause of Death, and Prescribed Drugs registers using the patients' social security numbers, which provided time of death and comorbidity data. The comorbidity data were used to calculate both the age-adjusted Charlson Comorbidity Index (CCI)[24] and the RCRI for each patient.[17]

BB THERAPY

The Swedish Prescribed Drugs Register, a population-based database that records all drug prescriptions issued by physicians in Sweden within both primary and secondary care facilities, was used to extract all issued BB prescriptions (ATC codes C07AA, C07AB, and C07AG). Ongoing BB therapy was defined as a patient having filled a prescription within the year before surgery. A period of 12 months was selected since BBs are rarely discontinued once initiated and therefore commonly issued on a long-term basis covering up to a 1-year period with a single prescription. β-Blockers are rarely discontinued in patients with hip fractures admitted for surgery; this assumption has previously been tested by assessing the electronic medical records of more than 2,400 consecutive hip fracture patients from one selected Swedish county during a 5-year period (between the years 2013 and 2017).[13] There were no statistically significant changes in BB prescription among the general population, for the same age group as the current study (≥65 years), during the study period.[25]

CALCULATING THE RCRI

The RCRI score was calculated using the variables defined by Lindenauer et al.[20]: high-risk surgery, ischemic heart disease, congestive heart failure, cerebrovascular disease, renal insufficiency, and diabetes mellitus, with each variable counting as one point if present. Hip fracture surgery is considered intermediate risk surgery according to the American College of Cardiology and the American Heart Association guidelines.[26] Accordingly, points for high-risk surgery were not awarded to any patient in this study.

STATISTICAL ANALYSIS

Initially, cases were grouped by their RCRI score of 0, 1, 2, 3, and ≥4, as presented by Lindenauer et al.[20] Cases were then further subdivided into ongoing β-blocker therapy (BB^+) and no β-blocker therapy (BB^-) at the time of admission, resulting in a total of 10 cohorts. Patient demographics and clinical characteristics were compared between the cohorts. Categorical variables were reported as counts with percentages, while continuous variables were reported as a mean and SD or median and interquartile range. Pearson's χ^2 test and Fisher's exact test were used to determine the statistical significance of differences between categorical variables. An analysis of variance was performed for normally distributed continuous variables; otherwise, a Kruskal-Wallis test was used. The primary outcome of interest was 30-day postoperative mortality.

Poisson regression analysis was used to study the association between BB therapy, the RCRI, and their interaction as they all relate to 30-day postoperative mortality. The regression analysis included BB therapy, RCRI, and their interaction as predictors (using the "*" notation available in the R formula interface) while adjusting for age, sex, ASA classification, type of surgery, fracture type, year of surgery, and comorbidities that were not included in the RCRI but were included in the CCI. Results are reported as incidence rate ratios (IRRs) with 95% confidence intervals (CIs). Statistical significance was defined as a two-sided p value of <0.05.

Less than 2% of patients had any missing data (Table 1). This is within the acceptable limits of what can be expected to be missing at random when working with retrospective data. Multiple imputation by chained equations was accordingly used to manage these missing values; logistic regression was used for sex, a proportional odds model for ASA classification, as well as Bayesian polytomous regression for type of fracture and type of surgery. This resulted in 10 imputed datasets. Analyses were performed using the statistical programming language R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 126,934 cases met the study inclusion criteria. From the 142,171 cases originally extracted from the Rikshöft register, 8,002 cases (5.6%) were excluded for being younger than 65 years, 2,877 cases (2.0%) were excluded because of incorrectly registered data, and 4,358 cases (3.1%) were excluded as they were reoperations. In the current study population, 40% of the patients (n = 50,673) were in the BB^+ cohorts, which is roughly equivalent to the 36% of people in the general geriatric population who have BB therapy during the same period.[25] Depicted in Table 1 are patient and clinical characteristics for each RCRI cohort, subdivided by BB exposure. Metoprolol was the most common BB used in all BB^+ cohorts. Patients with higher RCRI scores were less fit for surgery, based on their preoperative ASA score being ≥3 (BB^-: RCRI 0 vs. RCRI ≥4, 44.4% vs. 94.4%; $p < 0.001$) and had more comorbidities, based on their CCI score being ≥7 (BB^-: RCRI 0 vs. RCRI ≥4, 5.3% vs. 99.7%; $p < 0.001$). Total hip replacements were more commonly performed on patients with lower RCRI scores (BB^-: RCRI 0 vs. RCRI ≥4, 8.2% vs. 2.9%; $p < 0.001$) (Table 1).

All comorbidities increased with higher RCRI scores except for dementia, connective tissue disease, liver disease, and metastatic carcinoma (Table 2). The crude incidence of mortality 30 days postoperatively increased with each additional point on the RCRI (RCRI 0 to ≥4: 5.4%, 9.5%, 14.1%, 18.6%, and 22.1%). At the same time, postoperative mortality was significantly lower in BB^+ compared with BB^- patients within each RCRI cohort, irrespective of the specific cause of mortality (RCRI 0: BB^- vs. BB^+, 6.9% vs. 2.3%; RCRI ≥4: BB^- vs. BB^+, 53.6% vs. 8.8%; $p < 0.001$) (Table 3).

TABLE 1. Demographics

		RCRI 0		RCRI 1		RCRI 2		RCRI 3		RCRI ≥4		
	Total (N = 126,934)	BB⁻ (n = 50,457)	BB⁺ (n = 23,447)	BB⁻ (n = 18,971)	BB⁺ (n = 16,435)	BB⁻ (n = 5,221)	BB⁺ (n = 7,507)	BB⁻ (n = 1,296)	BB⁺ (n = 2,566)	BB⁻ (n = 306)	BB⁺ (n = 728)	*p*
Age, mean (SD)	84 (8)	83 (8)	84 (7)	84 (8)	84 (7)	85 (7)	84 (7)	85 (7)	83 (7)	84 (7)	82 (7)	<0.001
Sex, n (%)												<0.001
Female	87,933 (69.3)	36,439 (72.2)	18,062 (77.0)	12,078 (63.7)	11,412 (69.4)	2,824 (54.1)	4,650 (61.9)	587 (45.3)	1,428 (55.7)	122 (39.9)	331 (45.5)	
Male	38,987 (30.7)	14,011 (27.8)	5,381 (22.9)	6,893 (36.3)	5,021 (30.6)	2,397 (45.9)	2,857 (38.1)	709 (54.7)	1,137 (44.3)	184 (60.1)	397 (54.5)	
Missing	14 (0.0)	7 (0.0)	4 (0.0)	0 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	
Type of BB, n (%)												<0.001
Metoprolol	29,106 (22.9)	0 (0.0)	13,087 (55.8)	0 (0.0)	9,584 (58.3)	0 (0.0)	4,436 (59.1)	0 (0.0)	1,579 (61.5)	0 (0.0)	420 (57.7)	
Bisoprolol	9,551 (7.5)	0 (0.0)	3,526 (15.0)	0 (0.0)	3,278 (19.9)	0 (0.0)	1,829 (24.4)	0 (0.0)	685 (26.7)	0 (0.0)	233 (32.0)	
Atenolol	6,866 (5.4)	0 (0.0)	4,148 (17.7)	0 (0.0)	1,995 (12.1)	0 (0.0)	592 (7.9)	0 (0.0)	112 (4.4)	0 (0.0)	19 (2.6)	
Other	5,160 (4.1)	0 (0.0)	2,686 (11.5)	0 (0.0)	1,578 (9.6)	0 (0.0)	650 (8.7)	0 (0.0)	190 (7.4)	0 (0.0)	56 (7.7)	
None	76,251 (60.1)	50,457 (100.0)	0 (0.0)	18,971 (100.0)	0 (0.0)	5,221 (100.0)	0 (0.0)	1,296 (100.0)	0 (0.0)	306 (100.0)	0 (0.0)	
ASA classification, n (%)												<0.001
1	4,926 (3.9)	3,905 (7.7)	607 (2.6)	203 (1.1)	113 (0.7)	35 (0.7)	45 (0.6)	5 (0.4)	12 (0.5)	0 (0.0)	1 (0.1)	
2	44,884 (35.4)	23,153 (45.9)	10,308 (44.0)	5,535 (29.2)	3,878 (23.6)	736 (14.1)	974 (13.0)	80 (6.2)	177 (6.9)	8 (2.6)	35 (4.8)	
3	64,527 (50.8)	20,051 (39.7)	11,030 (47.0)	11,145 (58.7)	10,635 (64.7)	3,416 (65.4)	5,131 (68.3)	832 (64.2)	1,681 (65.5)	172 (56.2)	434 (59.6)	
4	10,159 (8.0)	2,328 (4.6)	1,049 (4.5)	1,730 (9.1)	1,514 (9.2)	944 (18.1)	1,223 (16.3)	358 (27.6)	655 (25.5)	113 (36.9)	245 (33.7)	
5	132 (0.1)	36 (0.1)	16 (0.1)	35 (0.2)	12 (0.1)	10 (0.2)	8 (0.1)	2 (0.2)	7 (0.3)	4 (1.3)	2 (0.3)	
Missing	2,306 (1.8)	984 (2.0)	437 (1.9)	323 (1.7)	283 (1.7)	80 (1.5)	126 (1.7)	19 (1.5)	34 (1.3)	9 (2.9)	11 (1.5)	
CCI, n (%)												<0.001
≤4	52,581 (41.4)	32,588 (64.6)	16,108 (68.7)	1,920 (10.1)	1,844 (11.2)	41 (0.8)	80 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
5–6	49,681 (39.1)	15,170 (30.1)	6,286 (26.8)	12,545 (66.1)	11,061 (67.3)	1,633 (31.3)	2,838 (37.8)	33 (2.5)	111 (4.3)	1 (0.3)	3 (0.4)	
≥7	24,672 (19.4)	2,699 (5.3)	1,053 (4.5)	4,506 (23.8)	3,530 (21.5)	3,547 (67.9)	4,589 (61.1)	1,263 (97.5)	2,455 (95.7)	305 (99.7)	725 (99.6)	
Type of fracture, n (%)												<0.001
Nondisplaced cervical (garden 1–2)	16,224 (12.8)	6,914 (13.7)	2,759 (11.8)	2,510 (13.2)	1,918 (11.7)	657 (12.6)	886 (11.8)	145 (11.2)	296 (11.5)	33 (10.8)	106 (14.6)	
Displaced cervical (garden 3–4)	47,344 (37.3)	18,755 (37.2)	8,825 (37.6)	7,051 (37.2)	6,120 (37.2)	1,927 (36.9)	2,837 (37.8)	481 (37.1)	961 (37.5)	116 (37.9)	271 (37.2)	
Basicervical	4,153 (3.3)	1,696 (3.4)	675 (2.9)	615 (3.2)	540 (3.3)	159 (3.0)	270 (3.6)	56 (4.3)	104 (4.1)	11 (3.6)	27 (3.7)	
Peritrochanteric (two fragments)	25,512 (20.1)	9,962 (19.7)	4,691 (20.0)	3,814 (20.1)	3,421 (20.8)	1,062 (20.3)	1,544 (20.6)	263 (20.3)	532 (20.7)	66 (21.6)	157 (21.6)	
Peritrochanteric (multiple fragments)	23,495 (18.5)	9,246 (18.3)	4,453 (19.0)	3,499 (18.4)	3,042 (18.5)	991 (19.0)	1,369 (18.2)	245 (18.9)	475 (18.5)	58 (19.0)	117 (16.1)	
Subtrochanteric	10,153 (8.0)	3,861 (7.7)	2,030 (8.7)	1,480 (7.8)	1,383 (8.4)	423 (8.1)	600 (8.0)	106 (8.2)	198 (7.7)	22 (7.2)	50 (6.9)	
Missing	53 (0.0)	23 (0.0)	14 (0.1)	2 (0.0)	11 (0.1)	2 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Type of surgery, n (%)												<0.001
Pins or screws	20,231 (15.9)	8,418 (16.7)	3,311 (14.1)	3,141 (16.6)	2,403 (14.6)	880 (16.9)	1,208 (16.1)	233 (18.0)	429 (16.7)	57 (18.6)	151 (20.7)	
Screws or pins with side plate	32,960 (26.0)	13,234 (26.2)	6,018 (25.7)	4,919 (25.9)	4,241 (25.8)	1,369 (26.2)	1,900 (25.3)	337 (26.0)	664 (25.9)	88 (28.8)	190 (26.1)	
Intramedullary nail	30,333 (23.9)	11,538 (22.9)	5,729 (24.4)	4,472 (23.6)	4,181 (25.4)	1,292 (24.7)	1,893 (25.2)	339 (26.2)	655 (25.5)	73 (23.9)	161 (22.1)	
Hemiarthroplasty	34,321 (27.0)	13,103 (26.0)	6,350 (27.1)	5,344 (28.2)	4,537 (27.6)	1,496 (28.7)	2,138 (28.5)	358 (27.6)	713 (27.8)	79 (25.8)	203 (27.9)	
Total hip replacement	9,016 (7.1)	4,134 (8.2)	2,026 (8.6)	1,084 (5.7)	1,064 (6.5)	178 (3.4)	365 (4.9)	28 (2.2)	105 (4.1)	9 (2.9)	23 (3.2)	
Missing	73 (0.1)	30 (0.1)	13 (0.1)	11 (0.1)	9 (0.1)	6 (0.1)	3 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	

BB⁻, no β-blocker therapy; BB⁺, ongoing β-blocker therapy.

TABLE 2. Preoperative Comorbidities

	RCRI 0		RCRI 1		RCRI 2		RCRI 3		RCRI ≥4		
	BB⁻ (n = 50,457)	BB⁺ (n = 23,447)	BB⁻ (n = 18,971)	BB⁺ (n = 16,435)	BB⁻ (n = 5,221)	BB⁺ (n = 7,507)	BB⁻ (n = 1,296)	BB⁺ (n = 2,566)	BB⁻ (n = 306)	BB⁺ (n = 728)	*p*
Myocardial infarction, n (%)	0 (0.0)	0 (0.0)	806 (4.2)	1,493 (9.1)	954 (18.3)	2,023 (26.9)	538 (41.5)	1,277 (49.8)	225 (73.5)	572 (78.6)	<0.001
Congestive heart failure, n (%)	0 (0.0)	0 (0.0)	3,951 (20.8)	5,105 (31.1)	2,818 (54.0)	4,645 (61.9)	1,098 (84.7)	2,169 (84.5)	296 (96.7)	703 (96.6)	<0.001
Hypertension, n (%)	10,102 (20.0)	9,582 (40.9)	8,415 (44.4)	9,887 (60.2)	3,027 (58.0)	5,266 (70.1)	890 (68.7)	2,010 (78.3)	251 (82.0)	632 (86.8)	<0.001
Arrythmia, n (%)	2,844 (5.6)	4,812 (20.5)	3,087 (16.3)	6,043 (36.8)	1,660 (31.8)	3,584 (47.7)	571 (44.1)	1,395 (54.4)	174 (56.9)	421 (57.8)	<0.001
Peripheral vascular disease, n (%)	1,150 (2.3)	790 (3.4)	902 (4.8)	976 (5.9)	470 (9.0)	687 (9.2)	166 (12.8)	361 (14.1)	74 (24.2)	141 (19.4)	<0.001
Cerebrovascular disease, n (%)	0 (0.0)	0 (0.0)	8,010 (42.2)	4,958 (30.2)	2,994 (57.3)	3,564 (47.5)	823 (63.5)	1,446 (56.4)	245 (80.1)	554 (76.1)	<0.001
Dementia, n (%)	11,598 (23.0)	3,324 (14.2)	5,224 (27.5)	3,043 (18.5)	1,375 (26.3)	1,405 (18.7)	328 (25.3)	484 (18.9)	68 (22.2)	138 (19.0)	<0.001
Chronic obstructive pulmonary disease, n (%)	4,593 (9.1)	1,976 (8.4)	2,671 (14.1)	2,147 (13.1)	949 (18.2)	1,345 (17.9)	283 (21.8)	547 (21.3)	82 (26.8)	172 (23.6)	<0.001
Connective tissue disease, n (%)	1,920 (3.8)	1,203 (5.1)	947 (5.0)	978 (6.0)	277 (5.3)	523 (7.0)	91 (7.0)	229 (8.9)	15 (4.9)	53 (7.3)	<0.001
Peptic ulcer disease, n (%)	1,169 (2.3)	583 (2.5)	683 (3.6)	641 (3.9)	268 (5.1)	403 (5.4)	91 (7.0)	174 (6.8)	23 (7.5)	57 (7.8)	<0.001
Liver disease, n (%)	296 (0.6)	163 (0.7)	215 (1.1)	169 (1.0)	54 (1.0)	85 (1.1)	28 (2.2)	29 (1.1)	4 (1.3)	13 (1.8)	<0.001
Diabetes, n (%)	0 (0.0)	0 (0.0)	5,376 (28.3)	4,142 (25.2)	2,564 (49.1)	3,349 (44.6)	780 (60.2)	1,652 (64.4)	251 (82.0)	633 (87.0)	<0.001
Hemiplegia, n (%)	142 (0.3)	68 (0.3)	741 (3.9)	575 (3.5)	312 (6.0)	385 (5.1)	85 (6.6)	150 (5.8)	23 (7.5)	73 (10.0)	<0.001
Chronic kidney disease, n (%)	0 (0.0)	0 (0.0)	828 (4.4)	737 (4.5)	1,112 (21.3)	1,433 (19.1)	649 (50.1)	1,154 (45.0)	237 (77.5)	548 (75.3)	<0.001
Local tumor, n (%)	4,829 (9.6)	2,332 (9.9)	2,390 (12.6)	1,998 (12.2)	800 (15.3)	1,026 (13.7)	210 (16.2)	368 (14.3)	62 (20.3)	110 (15.1)	<0.001
Metastatic carcinoma, n (%)	1,150 (2.3)	387 (1.7)	540 (2.8)	303 (1.8)	152 (2.9)	154 (2.1)	34 (2.6)	55 (2.1)	4 (1.3)	19 (2.6)	<0.001

BB⁻, no β-blocker therapy; BB⁺, ongoing β-blocker therapy.

TABLE 3. Crude Outcomes

	RCRI 0		RCRI 1		RCRI 2		RCRI 3		RCRI ≥4		
	BB⁻ (n = 50,457)	BB⁺ (n = 23,447)	BB⁻ (n = 18,971)	BB⁺ (n = 16,435)	BB⁻ (n = 5,221)	BB⁺ (n = 7,507)	BB⁻ (n = 1,296)	BB⁺ (n = 2,566)	BB⁻ (n = 306)	BB⁺ (n = 728)	*p*
Length of stay, median (IQR)	7 (5–11)	8 (5–12)	8 (5–12)	9 (5–13)	8 (5–12)	9 (5–13)	7 (4–11)	9 (6–13)	6 (4–12)	9 (5–14)	<0.001
Missing, n (%)	366 (0.7)	175 (0.7)	123 (0.6)	109 (0.7)	57 (1.1)	45 (0.6)	15 (1.2)	20 (0.8)	3 (1.0)	6 (0.8)	
30-d Cause, n (%)	3,476 (6.9)	535 (2.3)	2,700 (14.2)	652 (4.0)	1,340 (25.7)	451 (6.0)	499 (38.5)	220 (8.6)	164 (53.6)	64 (8.8)	<0.001
30-d Cause-specific mortality											
Cardiovascular event, n (%)	1,143 (2.3)	212 (0.9)	1,149 (6.1)	287 (1.7)	643 (12.3)	221 (2.9)	264 (20.4)	115 (4.5)	82 (26.8)	36 (4.9)	<0.001
Respiratory failure, n (%)	659 (1.3)	82 (0.3)	461 (2.4)	87 (0.5)	216 (4.1)	70 (0.9)	66 (5.1)	23 (0.9)	16 (5.2)	5 (0.7)	<0.001
Cerebrovascular event, n (%)	92 (0.2)	15 (0.1)	33 (0.2)	11 (0.1)	5 (0.1)	4 (0.1)	3 (0.2)	0 (0.0)	1 (0.3)	1 (0.1)	<0.001
Sepsis, n (%)	73 (0.1)	10 (0.0)	43 (0.2)	12 (0.1)	30 (0.6)	6 (0.1)	9 (0.7)	4 (0.2)	1 (0.3)	2 (0.3)	<0.001
Multiorgan failure, n (%)	1,340 (2.7)	191 (0.8)	929 (4.9)	225 (1.4)	423 (8.1)	134 (1.8)	142 (11.0)	73 (2.8)	63 (20.6)	19 (2.6)	<0.001
Unknown, n (%)	169 (0.3)	25 (0.1)	85 (0.4)	30 (0.2)	23 (0.4)	16 (0.2)	15 (1.2)	5 (0.2)	1 (0.3)	1 (0.1)	<0.001

Length of stay is measured in days.
BB⁻, no β-blocker therapy; BB⁺, ongoing β-blocker therapy; IQR, interquartile range.

TABLE 4. IRR for 30-day Mortality After Hip fracture Surgery

	IRR (95% CI)	*p*
BB therapy		
No	Reference	
Yes	0.35 (0.32–0.39)	<0.001
RCRI		
0	Reference	
1	1.57 (1.49–1.66)	<0.001
2	2.28 (2.13–2.43)	<0.001
3	3.00 (2.72–3.31)	<0.001
≥4	3.95 (3.36–4.65)	<0.001
BB therapy (BB^+) × RCRI*		
BB^+ × RCRI 1	0.87 (0.76–1.00)	0.046
BB^+ × RCRI 2	0.79 (0.68–0.92)	0.002
BB^+ × RCRI 3	0.81 (0.67–0.98)	0.027
BB^+ × RCRI ≥4	0.58 (0.42–0.79)	<0.001
Age	1.06 (1.06–1.07)	<0.001
Sex		
Female	Reference	
Male	1.66 (1.59–1.73)	<0.001
ASA classification		
1	Reference	
2	1.32 (1.09–1.61)	0.005
3	2.26 (1.86–2.75)	<0.001
4	3.78 (3.09–4.61)	<0.001
5	6.60 (4.73–9.21)	<0.001
Type of fracture		
Nondisplaced cervical (garden 1–2)	Reference	
Displaced cervical (garden 3–4)	1.29 (1.18–1.42)	<0.001
Basicervical	1.24 (1.05–1.46)	0.013
Peritrochanteric (two fragments)	1.24 (1.06–1.45)	0.006
Peritrochanteric (multiple fragments)	1.36 (1.16–1.59)	<0.001
Subtrochanteric	1.38 (1.17–1.63)	<0.001
Type of surgery		
Pins or screws	Reference	
Screws or pins with side plate	0.97 (0.84–1.12)	0.676
Intramedullary nail	0.93 (0.80–1.08)	0.369
Hemiarthroplasty	1.02 (0.94–1.10)	0.722
Total hip replacement	0.67 (0.57–0.79)	<0.001
Peripheral vascular disease		
No	Reference	
Yes	1.09 (1.00–1.19)	0.041
Chronic obstructive pulmonary disease		
No	Reference	
Yes	1.23 (1.16–1.30)	<0.001
Liver disease		
No	Reference	
Yes	1.70 (1.41–2.06)	<0.001
Dementia		
No	Reference	
Yes	1.41 (1.35–1.47)	<0.001
Connective tissue disease		
No	Reference	
Yes	1.01 (0.91–1.12)	0.835
Local tumor		
No	Reference	
Yes	1.09 (1.02–1.15)	0.007
Metastatic carcinoma		
No	Reference	
Yes	1.78 (1.61–1.98)	<0.001
Year of surgery		
2008	Reference	
2009	0.87 (0.79–0.97)	0.008
2010	0.94 (0.86–1.04)	0.234
2011	0.88 (0.80–0.96)	0.006
2012	0.95 (0.87–1.04)	0.278
2013	0.85 (0.77–0.93)	<0.001
2014	0.77 (0.70–0.85)	<0.001
2015	0.78 (0.71–0.86)	<0.001
2016	0.78 (0.71–0.86)	<0.001
2017	0.77 (0.70–0.85)	<0.001

Poisson regression model with robust standard errors of variance. Multiple imputation with chained equations was used to manage missing values. Model is adjusted for age, sex, peripheral vascular disease, chronic obstructive tissue disease, liver disease, dementia, connective tissue disease, local tumor, metastatic carcinoma, ASA classification, type of fracture, type of surgery, and year of surgery.

*The interaction between BB therapy and RCRI.

BB^-, no β-blocker therapy; BB^+, ongoing β-blocker therapy.

In the Poisson regression analysis, an increase in the RCRI score was associated with increased 30-day mortality risk after hip fracture surgery. There was a 57% increase in the postoperative mortality risk at RCRI 1 compared with RCRI 0 (adjusted [adj.] IRR [95% CI], 1.57 [1.49–1.66]; $p < 0.001$] and an almost fourfold increase at RCRI ≥4 compared with RCRI 0 (adj. IRR [95% CI], 3.95 [3.36–4.65]; $p < 0.001$) (Table 4).

β-Blocker therapy was associated with a 65% decrease in the risk of 30-day postoperative mortality in the whole study population (adj. IRR [95% CI], 0.35 [0.32–0.38]; $p < 0.001$). There was a statistically significant interaction between BB therapy and the RCRI. β-Blocker therapy was associated with an additional 13% reduction in mortality among patients with an RCRI score of 1 (adj. IRR [95% CI], 0.87 [0.76–1.00]; $p = 0.046$], while patients with an RCRI score of ≥4 exhibited an additional 42% reduction in postoperative mortality (adj. IRR [95% CI], 0.58 [0.42–0.79]; $p < 0.001$]. This suggests that the protective effect of BBs is even more important in patients with higher RCRI scores (Table 4).

DISCUSSION

This study, based on a total of 126,934 traumatic hip fracture cases, demonstrated a strong association between preoperative BB therapy and a reduced postoperative mortality risk in all RCRI cohorts. There was an enhanced and more pronounced mortality risk reduction by β-blockade exposure among patients with higher RCRI scores. Furthermore, patients in the highest risk strata, that is, RCRI ≥4, benefitted the most from BB therapy.

In Sweden, hip fractures occur in every fourth woman and every tenth man older than 50 years.[1] This results in approximately 18,000 hip fractures annually in Sweden; as the population continues to age, this number is expected to continue to grow.[1–4] These changes in population demographics are expected to result in an increased incidence of hip fractures worldwide.[27–30] Postoperative mortality rates as high as 10% after 30 days and up to 16% after 90 days following hip surgery have been reported.[2,5,7,8,27,31–33] Despite the implementation of several interventions during the last decades to reduce the mortality rate, including new orthopedic innovations, multidisciplinary care, and fast track programs that minimize time to surgery,[5,27,34,35] the postoperative mortality rate has largely been unaffected.[5,35]

The relationship between a high RCRI score and increased postoperative mortality has been demonstrated in several studies on patients undergoing noncardiac surgery along with more recent studies focusing on traumatic hip fractures, specifically.[18–21] This relationship was also observed in the currently studied population, where the incidence of mortality significantly increased with every additional point added to the RCRI score.

The association between BB therapy and a reduction in mortality after noncardiac surgery, including isolated hip fracture surgery, has been demonstrated previously.[9,11,13–15] The result of the current study suggests that geriatric patients with hip fractures could benefit from BB therapy. These results support current guidelines proposed by the American College of Cardiology in conjunction with the American Heart Association, as well as the European Society of Cardiology together with the European Society of Anesthesiology, which recommend considering the initiation of BB therapy in intermediate and high-risk patients (≥2 clinical risk factors, ASA class ≥3, or RCRI ≥3).[26,36] The majority of hip fracture patients fall within these defined risk groups. With this in mind, pharmaceutical treatment with BBs might be a reasonable next step in achieving a reduction in postoperative mortality in patients with hip fractures.

Despite having an RCRI score of 0, a large reduction in postoperative mortality risk was still seen in BB^+ patients in this cohort. This is not surprising since even this cohort contains older frail patients with a large number of comorbidities. In geriatric patients, who make up the majority of hip fracture patients, even those with RCRI 0 are likely to have some degree of cardiovascular comorbidity despite not having a formal diagnosis. However, the most pronounced effect of BB therapy was seen in patients with an RCRI score greater than 0, that is, patients who have an even greater comorbidity burden.

β-Blockers have during the past years fallen out of favor with clinicians as a result of studies such as the PeriOperative ISchemic Evaluation (POISE) trial.[37] Although the POISE trial showed a decrease in adverse cardiac events among patients who received preoperative BBs, their use was associated with an increased risk of stroke and overall mortality.[37] The POISE trial was, however, limited by the heterogeneity in the patient population, making no distinction between those subjected to vascular, orthopedic, and general abdominal surgical procedures, along with the unusually high dose of BBs administered to previously BB-naive patients. While randomized controlled trials are considered the criterion standard for evidence in the medical field, observational studies have also been demonstrated to be of comparable value when other factors besides study design, such as external validity and sample sizes, are considered.[38] At the moment, there are still many questions regarding the initiation of preoperative BB therapy in noncardiac surgery, but with the publication of several large observational studies during the past years, the consensus appears to once again have shifted to BBs potentially having a beneficial effect, at the very least in patients with a high cardiac risk.[39]

This study benefits from using consecutive data from a nationwide database, well known for its high case coverage.[40] Despite this strength, there are several limitations that need to be acknowledged. Including only cases from Sweden may limit the external validity of these results, but it can also be considered a strength, as the access to universal health care results in a more homogenous sample population. Because of the retrospective nature of the study, estimation of the severity of renal impairment through calculation of Acute Kidney Injury Network or Kidney Disease Improving Global Outcomes scores was not possible. We therefore elected to use the documentation of chronic kidney disease diagnosis using *International Classification of Diseases, Ninth and Tenth Revision*, codes as a surrogate, as originally described by Lindenauer et al.[20] Changes to BB therapy perioperatively could not be determined in the current study, as this is not recorded in any Swedish quality register. However, a review of 2,443 cases treated for traumatic hip fractures in the Swedish county of Orebro found that no patient with BB therapy before surgery had this treatment discontinued during their stay in the hospital.[13] This is also in line with current medical guidelines for BB therapy.[26,36] Furthermore, data regarding other drugs, which may have affected outcomes, was not collected and independently studied, since it was outside of the scope of the current study. Finally, the clustering effects attributable to the treating facility could not be accounted for, since the treating facility was not listed in the dataset used. However, hip fracture management is relatively homogenous in Sweden; management is based on national guidelines, and the choice of intervention and follow-up is primarily based on the morphology of the hip fracture rather than an individual surgeon's preferences.

CONCLUSION

In conclusion, the preoperative prescription of BBs was associated with a significant reduction in 30-day postoperative mortality within all RCRI cohorts, with the greatest survival benefit seen in patients with the highest cardiac risk. These findings may be beneficial to surmounting the challenge of reducing mortality after hip fracture surgery. Additional prospective studies are warranted to explore this relationship.

AUTHORSHIP

A.M.I. contributed in the study design, data collection, data analysis, interpretation of data, and drafting of article. R.A. contributed in the study design, interpretation of data, and drafting of article. M.P.F. contributed in the data analysis, interpretation of data, and drafting of article. Y.C. contributed in the data analysis, interpretation of data, and critical revision of article. P.W. contributed in the interpretation of data and critical revision of article. T.B. contributed in the interpretation of data and critical revision of article. S.M. contributed in the study design, data collection, data analysis, interpretation of data, and critical revision of article. All authors have read and approved the article submitted.

DISCLOSURE

The authors declare no conflicts of interest.
The abstract of this article has been accepted for a podium (quick shot) presentation at the 80th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery to be held in Atlanta, Georgia on September 28 to October 2, 2021.
Ethical approval was obtained from the Swedish Ethical Review Authority (reference 2021-01744). Because of the retrospective nature of the study, formal consent was not required from patients included in the current study. The data sets and codes used during the current study are available from the corresponding author on reasonable request from the editorial board.

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