Clinical and Experimental
Health Sciences

The Effect of HbA1c Level on Gender-Specific Long-Term Morbidity and Mortality After Isolated Coronary Bypass in Poorly Controlled Diabetic Patients

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Received: 20.08.2020 **Accepted:** 11.02.2021

ABSTRACT

Objective: The aim of this study is to evaluate the gender specific effects of the high HbA1c levels in poorly controlled diabetic patients undergoing isolated coronary artery bypass grafting (CABG) procedure on long term morbidity, mortality and re-revascularization (2nd intervention).

Methods: This study was conducted on 532 (346 (65%) males and 186 (35%) females) diabetic patients who underwent CABG procedure at a single center between January 2010 and December 2013.The patients were separated into 4 groups according to gender and preoperative HbA1c level (%). The group1 consisted of females with HBA1c level ≤7(n=46); the group 2 comprised female with HbA1c level >7(n=140); the group 3 comprised men with HbA1c level ≤7(n=117); and the group 4 comprised men with HbA1c level >7(n=229). The groups were analyzed and compared for postoperative complications and mortality.

Results: No statistically significant difference was found among the groups in HbA1c levels and gender with respect to postoperative infection and mortality (p>0.05). The HbA1c level was determined to be statically significant and required the 2nd intervention (p:0.001; 95% CI: 1.249 (1.055,1.478)).

Conclusion: This study suggested that there was no difference in mortality rates after CABG among the groups although the current risk calculator modules stated otherwise. However, the HbA1c levels were associated with a need for a secondary intervention on long term follow up period.

Keywords: Diabetes Mellitus, Coronary Artery Bypass Grafts, Gender

1. INTRODUCTION

The ratio of diabetes mellitus (DM) was 23% among patients undergoing coronary artery bypass graft (CABG)surgery. This percentage is higher in female and currently increasing in both genders [1-3]. Diabetic patients have 2-4 fold higher mortality rate associated with cardiovascular disease as compared with non-diabetic patients, and the morbidity rate is also higher [4].

Hemoglobin A1c (HbA1c) is commonly used as an indicator of long-term average blood glucose levels [5]. HbA1C is an approved criterion for diagnosis of DM by The American Diabetes Association [6]. Higher levels of HbA1c (> 7%) have been found to be related to various complications (stroke, myocardial infarction) and increased risk of all-cause mortality following open heart surgery, but gender specific effects of higher levels of HbA1c are not well sought [7].

In this study, poorly controlled diabetic patients undergoing CABG surgery were retrospectively analyzed. The effect of gender and higher HbA1c levels on the long term morbidity, mortality and the need for repeat revascularization were studied.

2. METHODS

This study was conducted on a total of 532 diabetic cases comprising 346 (65%) men and 186(35%) female who underwent isolated CABG at a single center between January 2010 and December 2013. The mean age of the patients was 60.26±9.32 years (range, 31-84 years).

The Inclusion criteria were as follows: being diagnosed with uncontrolled diabetes (HbA1c > 5,6 %), receiving any kind of treatment for diabetes and undergoing isolated CABG surgery. The patients were separated into 4 groups according to gender and HbA1c levels. The threshold pre-operative HbA1c level of 7% was accepted as a marker of uncontrolled diabetes, according to the current literature [7,8]. The group 1 comprised of female with HBA1c level≤ 7% (n=46); the group 2 comprised of female with HBA1c level >7% (n=140); the group 3 comprised of men with HBA1c level≤ 7% (n=117); and the group 4 comprised of men with HBA1c level > 7% (n=229). Additionally, we evaluated the clinical progress of

ISSN:2459-1459

DOI: 10.33808/clinexphealthsci.782816

the symptoms of coronary artery disease (CAD) in the long term follow up period. The asymptomatic patients had no recurrent symptoms of coronary artery ischemia at follow-ups. The symptomatic patients were those who presented with symptoms of coronary artery disease and underwent coronary angiography but did not require revascularization. Symptomatic patients (n: 66, 12.4%) who had required re-revascularization were classified as the second intervention patients receiving treatment either with redo CABG or PCI (n: 41, 7.7%). Three of symptomatic patients required redo CABG.

Long-term survival results were searched on hospital database, the national health database and phone-calls with the patients. Also, potential second intervention to the patient in another institution was interrogated during these phone-calls. If the second intervention history is positive, detailed information of this second intervention was obtained from the host-institute by phone-calls too. We excluded the patients with the missing data.

The exclusion criteria were as follows: non-diabetic patients and diabetic patients with low HbA1c level (HbA1c 5,6%) patients with incomplete medical reports, patients using steroids or undergoing chemotherapy, and those receiving a diagnosis of decompensated congestive heart failure, congenital heart disease, cerebrovascular disease within the previous 30 days, dialysis-dependent kidney failure, a clinically active malignancy, endocrinological disorders (hypothyroidism, hyperthyroidism), systemic inflammatory disease, hematological proliferative disease, low hemoglobin levels (Hgb ≤ 10 g/dl), a clinically active infection, or a diagnosis of autoimmune disease.

After the local ethical committee approval, the demographic and clinical characteristics were recorded for each patient. Acute kidney injury (AKI) was evaluated and classified according to the Kidney Disease Improving Global Outcomes (KDIGO) classification by calculating preoperative and postoperative serum creatinine levels [9]. Chronic obstructive pulmonary disease (COPD) was defined as follows: – Patients with obstructive pattern in preoperative spirometry (FEV1/FEVC<0,70). –Patients having active treatment for COPD [10].

DM was accepted as the use of oral anti-diabetic drugs or insulin or a fasting blood glucose level > 126 mg/dl [11]. Before the procedure, peripheral venous blood samples (5-7 cc) were obtained and placed in sterile EDTA tubes to prevent clotting. After 1 hour, hematological parameters were calculated with an automatic blood count device (Abbott CELL-DYN 3700; Abbott Laboratory, Abbott Park, Illinois, USA). All patients had oral antidiabetic-drug or insulin. No patient among all 4 groups received both insulin and oral diabetic drugs at the same time. We evaluated preoperative low density lipoprotein level (LDL > 100 mg/dl and >190 mg/dl) (12).

2.1. Blood Sugar Examinations

Throughout the operation, the blood glucose levels of the patients were evaluated once before the CPB and then at hourly intervals. Crystallized insulin (Humulin R®, Lilly, Indianapolis, USA) was applied intravenously to control blood glucose level. In the intensive care unit (ICU), all patients' blood glucose levels were regulated with an insulin infusion according to the Portland protocol [13]. An average glucose level was calculated for each patient.

2.2. Surgical procedure

All the surgical procedures were performed as on or off pump during CABG surgery. Following the anesthesia induction median sternotomy was performed in all of the patients. Coronary bypass grafts were harvested from the saphenous vein and the left internal mammary artery (pediculate). A non-pulsatile roller pump and membrane oxygenator was used for cardiopulmonary bypass (CPB) in on-pump CABG patients. The surgical procedure was performed at moderate systemic hypothermia (28°C-30°C). CPB was applied at a flow rate of 2.2-2.5 L/min/m^2. Mean arterial pressure between 50-80 mmHg and hematocrit values of 20%-25% were achieved in all patients. Myocardial protection was applied with intermittent antegrade and continuous retrograde hypothermic and hyperkalemic blood cardioplegia. The proximal anastomoses were performed on beating heart under a partial clamp. Additionally; electrocardiogram (ST segments), mean arterial pressure (>70mmHg), cardiac output and activated clotted time (ACT > 250 seconds) monitored continuously during the off-pump CABG procedure.

2.3. Statistical Analyses

For the statistical analysis, NCSS 2007 software was used (Number Cruncher Statistical System, Kaysville, Utah, USA). Descriptive statistical methods such as mean, standard deviation, median, the first quartile, the third quartile, frequency, and percentage, minimum, maximum were used for reporting the data. Independent samples t-test was used to compare normally distributed variables between the 2 groups, Mann-Whitney U-test was used for variables violating normal distribution assumption. One-way ANOVA with Tukey HSD post hoc tests were used to compare normally distributed variables between 3 or more groups. Kruskal-Wallis test with Dunn-Bonferroni post hoc tests were used to compare non-normally distributed variables between 3 or more groups. The Pearson chi-square test, the Fisher-Freeman-Halton exact test, the Fisher's exact test were used to compare qualitative data. Pearson correlation analysis was used to assess the correlation between quantitative variables. The effects of risk factors on postoperative infection and mortality were evaluated via binary backward logistic regression analysis, whereas effects of risk factors on the second intervention were evaluated via multivariate backward logistic regression analysis. The effects of risk factors on length of ICU stay, length of hospital stay and chest tube output were evaluated via linear regression analysis. A p value of <0.05 was accepted as statistically significant.

4. RESULTS

The distributions of the descriptive, the preoperative and postoperative characteristics are shown in Table 1. Among 532 cases included in the study, 467 (87.8%) survived, and 65 died. The CABG procedures were performed with on-pump procedure in 471 patients and on off-pump strategy in 61 patients.

The mean survival time was 72.29±1.00 months. The latest death occurred at 77.1 months, and in that month, the cumulative survival rate was 86.1%, with a standard error of 2.0%. These results are shown according to groups in Figure 1.

Table 1. *Comparison according to Gender& HbA1c levels*

		Total (n=532)	Female & HbA1c≤%7 (n=46)	Female & HbA1c>%7 (n=140)	Male & HbA1c≤%7 (n=117)	Male & HbA1c>%7 (n=229)	P
Gender	Female	186 (35)	46 (100)	140 (100)	0 (0)	0 (0)	-
	Male	346 (65)	0 (0)	0 (0)	117 (100)	229 (100)	
HbA1c (%)		8,74±1,74	6,880±0,29	9,58±1,6	6,98±0,27	9,47±1,5	-
Age (years)		60,26±9,32	61,87±8,55	62,08±9,05	61,15±9,7	58,36±9,13	a0,001*
BMI (kg/m²)		29,3±4,82	31,15±6,11	29,95±5,37	29,19±4,47	28,58±4,19	a0,002*
Previous MI		223 (41,9)	14 (30,4)	61 (43,6)	44 (37,6)	104 (45,4)	b0,196
COPD		73 (13,7)	3 (6,5)	22 (15,7)	21 (17,9)	27 (11,8)	b0,174
Hypertension		300 (56,4)	34 (73,9)	98 (70)	66 (56,4)	102 (44,5)	b<0,001*
PVD		26 (4,9)	1 (2,2)	3 (2,1)	6 (5,1)	16 (7)	b0,159
EF (%)		54,02±11,15	57,8±9,44	55,5±10,39	54,71±11,12	52,01±11,59	a0,001*
LDL > 100; n (%)		335(65,6)	33 (73.3)	87 (63)	84 (73.7)	131 (60.1)	c0.053
LDL > 190; n (%)		34(6,6)	3 (6.7)	7 (5.1)	9 (7.9)	15 (6.9)	c0.835
Critical stenosis		6 (1,1)	0 (0)	2 (1,4)	0 (0)	4 (1,7)	c0,574
LIMA used		484 (91)	41 (89,1)	128 (91,4)	107 (91,5)	208 (90,8)	b0,967
Reoperation		11 (2,1)	1 (2,2)	5 (3,6)	2 (1,7)	3 (1,3)	c0,463
DM treatment	OAD	403 (75,8)	39 (84,8)	89 (63,6)	101 (86,3)	174 (76)	b<0,001*
	Insulin	129 (24,2)	7 (15,2)	51 (36,4)	16 (13,7)	55 (24)	
AKI	0	357 (67,1)	28 (60,9)	83 (59,3)	85 (72,6)	161 (70,3)	b0,061
	1	175 (32,9)	18 (39,1)	57 (40,7)	32 (27,4)	68 (29,7)	
Length of ICU stay (hours)		44 (25-69)	47,5 (25-95)	41 (23-49)	46 (24-75)	46 (24-72)	d0,010*
Length of hospitalstay (days)		7,5 (6-12)	8 (7-11)	7 (6-10)	7 (7-11)	7 (7-11)	d0,251
Followupperiod (months)		50,9 (43,5-68,4)	54,07 (43,65-71,08)	57,27 (42,73-71,5)	54,67 (42,5-69,33)	55,13 (42,87-69,93)	d0,867
Intubationduration (hours)		11 (8-16)	11,5 (8-16)	9 (8-12)	10 (8-13)	10 (8-13,5)	d0,004*
Number of distal bypass grafts		3 (2-3)	3 (2-3)	3 (2-3)	3 (2-4)	3 (2-3)	d0,008*
Chesttubeoutput (ml)		550 (400-700)	450 (350-600)	550 (450-800)	600 (450-800)	550 (400-775)	d<0,001*
Perfusionduration (minutes)		82,5 (49-94)	91 (64-115,5)	81 (58-102)	90 (62-112)	88 (61,5-109,5)	d0,076
ACC (minutes)		48,5 (30-64)	50 (33,5-70)	48 (30-64)	52 (35-70)	50 (33-68)	d0,249
Post-op infection		56 (10,5)	4 (8,7)	20 (14,3)	11 (9,4)	21 (9,2)	b0,412
Mortality		65 (12,2)	5 (10,9)	21 (15)	13 (11,1)	26 (11,4)	b0,710
2nd Intervention	**Symptomatic (-)**	425 (79,9)	37 (80,4)	106 (75,7)	98 (83,8)	184 (80,3)	b0,300
	Symptomatic (+)	66 (12,4)	5 (10,9)	17 (12,1)	15 (12,8)	29 (12,7)	
	2nd Intervention	41 (7,7)	4 (8,7)	17 (12,1)	4 (3,4)	16 (7)	

*BMI: Body Mass Index, MI: Myocardial Infarction, COPD: Chronic Obstructive Pulmonary Disease, PVD: Peripheral Vascular Disease, EF: EjectionFraction, HbA1c: Glycosylated Hemoglobin, LIMA: Left Internal Mammarian Artery, DM: Diabetes Mellitus ICU:Intensive Care Unit, ACC: Aortic Cross Clamp AKI: Acutekidneyinjury LDL: Low Dansity Lipoprotein; aOne-way ANOVA (reported as mean±sd); bPearsonchi-square test (reported as n (%)); cFisher-Freeman-Haltonexact test (reported as n (%)); dKruskal-Wallis test (reported as median (Q1-Q3)); Q1:First quartile, Q3:Third quartile; *p<0,05*

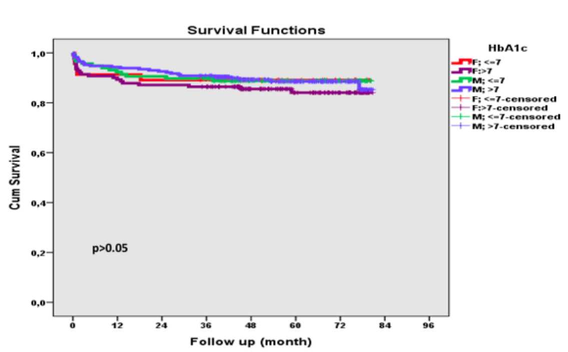

Figure 1. *Survival graphic according to HbA1c levels*

No statistically significant difference was determined among the groups regarding postoperative infection, mortality and the 2nd intervention (p>0.05). The AKI, age, COPD, the length of ICU and the number of distal bypass grafts were found to be statistically significant in mortality (p<0.05). The length of hospital stay was significantly associated with infection (p<0.05). There were no statically significant differences in LDL parameters among the groups (p<0.05).

The postoperative infection, mortality and the 2nd intervention were evaluated according to the characteristics (shown in Table 2).

Table 2. *The patients'scharacteristics determined mortality, infection and the second intervention*

		PostopInfection			Mortality			2ndIntervention			
		No	Yes	P	No	Yes	P	S (-)	S (+)	2ndInt.	p
Age (years)		60,12±9,29	61,45±9,54	[e]0,313	59,5±8,95	65,71±10,15	[e]<0,001*	60,48±9,29	60,17±9,18	58,12±9,82	[a]0,303
BMI (kg/m^2)		29,25±4,8	29,66±5,04	[e]0,553	29,28±4,73	29,38±5,5	[e]0,887	29,28±4,87	29,06±4,06	29,86±5,49	[a]0,697
Previous MI	No	268 (86,7)	41 (13,3)	[b]0,015*	270 (87,4)	39 (12,6)	[b]0,738	250 (80,9)	36 (11,7)	23 (7,4)	[b]0,778
	Yes	208 (93,3)	15 (6,7)		197 (88,3)	26 (11,7)		175 (78,5)	30 (13,5)	18 (8,1)	
COPD	No	415 (90,4)	44 (9,6)	[b]0,076	410 (89,3)	49 (10,7)	[b]0,006*	367 (80)	55 (12)	37 (8,1)	[b]0,597
	Yes	61 (83,6)	12 (16,4)		57 (78,1)	16 (21,9)		58 (79,5)	11 (15,1)	4 (5,5)	
Hypertension	No	208 (89,7)	24 (10,3)	[b]0,905	207 (89,2)	25 (10,8)	[b]0,372	187 (80,6)	30 (12,9)	15 (6,5)	[b]0,625
	Yes	268 (89,3)	32 (10,7)		260 (86,7)	40 (13,3)		238 (79,3)	36 (12)	26 (8,7)	
PVD	No	453 (89,5)	53 (10,5)	[g]0,747	445 (87,9)	61 (12,1)	[g]0,544	403 (79,6)	63 (12,5)	40 (7,9)	[c]0,932
	Yes	23 (88,5)	3 (11,5)		22 (84,6)	4 (15,4)		22 (84,6)	3 (11,5)	1 (3,8)	
EF (%)		53,94±11,28	54,77±10	[e]0,598	54,27±11,27	52,28±10,13	[e]0,178	54,28±11,03	51,44±11,93	55,51±10,68	[a]0,105
Critical stenosis	No	470 (89,4)	56 (10,6)	[g]0,999	462 (87,8)	64 (12,2)	[g]0,544	420 (79,8)	66 (12,5)	40 (7,6)	[c]0,491
	Yes	6 (100)	0 (0)		5 (83,3)	1 (16,7)		5 (83,3)	0 (0)	1 (16,7)	
LIMA used	No	42 (87,5)	6 (12,5)	[b]0,640	41 (85,4)	7 (14,6)	[b]0,600	38 (79,2)	9 (18,8)	1 (2,1)	[b]0,144
	Yes	434 (89,7)	50 (10,3)		426 (88)	58 (12)		387 (80)	57 (11,8)	40 (8,3)	
Reoperation	No	467 (89,6)	54 (10,4)	[g]0,325	458 (87,9)	63 (12,1)	[g]0,632	417 (80)	65 (12,5)	39 (7,5)	[c]0,334
	Yes	9 (81,8)	2 (18,2)		9 (81,8)	2 (18,2)		8 (72,7)	1 (9,1)	2 (18,2)	
DM treatment	OAD	363 (90,1)	40 (9,9)	[b]0,425	357 (88,6)	46 (11,4)	[b]0,317	327 (81,1)	51 (12,7)	25 (6,2)	[b]0,071
	Insulin	113 (87,6)	16 (12,4)		110 (85,3)	19 (14,7)		98 (76)	15 (11,6)	16 (12,4)	
AKI	0	327 (91,6)	30 (8,4)	[b]0,023*	330 (92,4)	27 (7,6)	[b]<0,001*	284 (79,6)	43 (12)	30 (8,4)	[b]0,666
	1	149 (85,1)	26 (14,9)		137 (78,3)	38 (21,7)		141 (80,6)	23 (13,1)	11 (6,3)	
Intubationduration (hours)		10 (8-13)	12 (8-17)	[f]0,035*	10 (8-13)	11 (8-18)	[f]0,103	10 (8-14)	10 (8-12)	9 (8-12)	[d]0,369
Number of distal bypass grafts		3 (2-3)	3 (2-4)	[f]0,329	3 (2-3)	3 (1-3)	[f]0,028*	3 (2-3)	2 (1-3)	3 (2-4)	[d]0,012*
Perfusionduration (minutes)		87 (60-108)	97,5 (78,5-116,5)	[f]0,023*	88 (63-110)	90 (40-109)	[f]0,686	90 (64-110)	68,5 (47-95)	87 (64-108)	[d]0,005*
ACC (minutes)		49 (32-67,5)	56 (43-70)	[f]0,141	50 (35-68)	52 (20-70)	[f]0,607	51 (35-69)	43,5 (20-64)	51 (38-65)	[d]0,044*
Length of ICU stay (hours)		45 (24-71)	47,5 (25-97,5)	[f]0,060	45 (24-70)	51 (23-119)	[f]0,031*	47 (24-72)	44 (24-52)	42 (24-71)	[d]0,606
Length of hospitalstay (days)		7 (6-10)	13 (8-18,5)	[f]<0,001*	7 (7-10)	11 (7-19)	[f]<0,001*	7 (7-11)	8 (7-10)	8 (7-11)	[d]0,360
Chesttubeoutput (ml)		550 (400-800)	550 (425-700)	[f]0,894	550 (400-750)	550 (350-800)	[f]0,610	550 (400-800)	550 (400-700)	600 (450-900)	[d]0,300

*BMI: Body Mass Index, MI: Myocardial Infarction, COPD: Chronic Obstructive Pulmonary Disease, PVD: Peripheral Vascular Disease, EF: Ejection Fraction, HbA1c: Glycosylated Hemoglobin, LIMA: Left Internal Mammarian Artery, DM: Diabetes Mellitus ICU: Intensive Care Unit, ACC: Aortic Cross Clamp AKI: Acutekidneyinjury , S+ : patients who had symptoms of coronary artery disease; [a]One-way ANOVA (reported as mean±sd); [b]Pearsonchi-square test (reported as n (%)); [c]Fisher-Freeman-Haltonexact test (reported as n (%)); [d]Kruskal-Wallis test (reported as median (Q1-Q3)); [e]Independentsamples t test (reported as mean±sd); [f]Mann-Whitney U test (reported as median (Q1-Q3)); [g]Fisher'sexact test (reported as n (%)); Q1:First quartile, Q3:Third quartile; *p<0,05*

There was a statistically significant difference in the need for the second intervention according to number of distal bypass grafts (p<0.05). Also, the patients with the high HbA1c levels required a higher rate of intervention with time (p<0.05). There was no statistically significant difference in the need for re-intervention between off-pump (n: 3, 4.9%) and on-pump (n: 38, 8.1%) procedures (p=0.066).

The risk factors of postoperative infection and mortality were determined with binary logistic regression and for the 2nd intervention with multivariate logistic regression analysis. Gender, HbA1c and variables with p<0.150 in gender comparisons (age, BMI, HT, PVD, EF, DM treatment, AKI, length of ICU stay, Intubation duration, distal bypass grafts, chest tube output and length of hospital stay) were included as independent variables. In addition to these variables, for each dependent variable, the variables with p<0.150 in the uni-variable analysis regarding that variable were also included in the corresponding model (Table 3).

The model for postoperative infection was found to be statistically significant (χ^2=33.169, p<0.001). Previous MI and length of hospital stay were found to have significant effect on postoperative infection (p=0.022, p<0.001, respectively).

The model for mortality was found to be statistically significant (χ^2=70.242, p<0.001). Age, AKI, length of ICU stay, COPD and number of distal bypass grafts were found to have significant effect on mortality (p<0.001, p<0.001, p<0.001, p=0.043, p=0.005, respectively).

It was found that the model for the 2nd intervention was statistically significant (χ^2=15.862, p=0.003). HbA1c level and number of distal bypass grafts were found to have significant effect on the 2nd intervention (p=0.010, p=0.003, respectively). The one unit changes of HbA1c levels can increase the 2nd intervention risk by 1.249 times.

Table 3. *Logistic regression analyses according to infection, mortality and 2nd intervention*

Dependentvariable		Independentvariables	p	OR (95% CI)
Postopinfection		Constant	<0.001*	0.066
		Previous MI (no)	0.022*	2.116 (1.113, 4.024)
		Length of hospitalstay	<0.001*	1.072 (1.042, 1.103)
Mortality		Constant	<0.001*	0.012
		Age	<0.001*	1.07 (1.036, 1.104)
		AKI (1)	<0.001*	2.905 (1.626, 5.193)
		Length of ICU stay	<0.001*	1.006 (1.003, 1.009)
		COPD (yes)	0.043*	2.074 (1.022, 4.208)
		Number of distal bypass grafts	0.005*	0.667 (0.502, 0.885)
2nd intervention	Symptomatic (+)	Intercept	0.042*	-
		HbA1c	0.347	1.075 (0.924, 1.251)
		Number of distal bypass grafts	0.003*	0.677 (0.523, 0.876)
	2nd intervention	Intercept	<0.001*	-
		HbA1c	0.010*	1.249 (1.055, 1.478)
		Number of distal bypass grafts	0.995	0.999 (0.733, 1.362)

*MI: Myocardial Infarction, COPD: Chronic Obstructive Pulmonary Disease, HbA1c: Glycosylated Hemoglobin, ICU: Intensive Care Unit, AKI: Acute kidney injury; OR: Odds Ratio; CI: Confidence Interval; Sypmtomatic (-) wastaken as the reference category for the 2nd Intervention analysis; *p<0.05*

5. DISCUSSION

In this study, the effect of the HbA1c level was investigated on long-term morbidity, mortality and the need for the second intervention following CABG procedure in poorly controlled diabetic patients with respect to male and female patients. The results of the study showed that there was no difference in mortality rates after coronary bypass among the groups with respect to HbA1c level and gender. However, there was a significantly higher need for the second intervention among patients with high HbA1c level on long term follow up period.

Hyperglycemia has been shown to expand the infarct field in the myocardium, to impair ischemic preconditions and to increase reperfusion injury [14]. Compared to non-diabetic individuals, diabetic patients are known to have a higher morbidity and mortality rate in coronary artery disease (CAD) [15,16]. Diabetes is also an indicator of the development of atherosclerosis and plaque instability. Therefore, and specific to diabetes, the number of vessels affected in CAD is usually more than one, the coronary diameters are small, lesion locations are usually osteal or proximal and completely obstructed, narrowing is more often in the left main artery [6,17], collateral vessel development is impaired [18], and there is greater coronary artery calcification [19]. Similarly, females have coronary arteries of a smaller diameter. Small coronary arteries are more predisposed to occlusion and spasm [20]. The most common cause of death of females worldwide is CAD [21]. However, CAD is seen more often as a male disease than female disease [22]. In the past 10 years, there has been a marked increase in CABG operations in females, and currently, 1 out of every 3 CABG operations is performed on a female patient[23].In this study, females comprised 35% of the study groups. We did not determined difference among the four groups regarding mortality and the 2ndintervention.

In a study by Blankstein et al. who investigated the mortality rates in females, it was reported that female gender was independent risk factors for mortality after CABG. [24]. Ennker et al. stated that there was no effect of gender related to increased risk of CABG operation among females [25]. In our study, gender did not have any effect on mortality rates.

In our study, based on gender, the mortality rates were 13,9% for the female group and 11,2% for the male group, it was not statically different contrary to the widely accepted risk calculators [19,24]. Additionally, the length ICU stay and chest tube output were found to be longer for female patients than for the male patients.

Hemoglobin A1c (HbA1c) is an index of long-term average blood glucose levels and outcome predictors in diabetic patients [5,7]. Higher levels of HbA1c have been associated increased major adverse cardiac events and death (7,26). Halko et al. studied 3089 diabetic and non-diabetic patients in a prospective study and they found that HbA1c levels had significant effect on hospital stay, morbidity and mortality. Mortality was found to be increased in those with high HbA1c, ≥8.6% [27]. Robich et al., found poor long-term survival in increased HbA1c among patients undergoing CABG (ratio of death risk increased by %13 for every unit increase in HbA1 [28]. Nystrom and colleagues found that high levels of HbA1c resulted in increased rates of mortality and repeat revascularization on type 1 diabetic patients who underwent CABG within 4,7 years follow up (29). In this study, there was no difference between the groups according HbA1c levels (HbA1c >7: 12, 7%; HbA1c <7: 11, 0%) for long term mortality. Also one of the findings of this study was that there was a statistically significant higher requirement for the secondary revascularization following coronary bypass in patients who had a high level of HbA1c. Revascularization was provided for these patients following angiography. According to the clinical status of the patients, the revascularization was performed as an angiographic procedure or as a redo CABG.

Some other parameters such as preoperative ventricular function can affect early outcome after CABG (30). We did not observe any effect of EF on adverse outcomes, including mortality.

Previous studies have reported that sternal complications are high in DM patients following CABG operations and that this rate can increase to 10% [31] and the level of HbA1c is associated with sternal wound infection (32). Halkos et al. also reported that mortality and sternal infection rates increased with a high HbA1c level [27]. In the current study, contrary to expectations, no statically difference was observed in infection rates with respect to the HbA1c level and gender among the selected diabetic groups.

Czech et al. examined 2881 DM patients undergoing CABG operation and determined that rates of mechanical ventilation were higher and the length of stay in the ICU was longer in females [19]. In this study, all the patients had DM, and the lengths of stay in the ICU and in the hospital were determined to be statistically significantly longer in females with a high HbA1c level compared to the other groups. Additionally, we found that level of HbA1c were a risk factor for drainage.

Some studies showed that high level of HbA1c and diabetes mellitus was associated with increased postoperative AKI after CABG [33-34]. According to the KDIGO 2012 AKI Guidelines, cardiac surgery with CPB is a 1B risk factor (9). Although there is no consensus on AKI and Hba1c levels in patients with no known renal disease, HbA1c of>7% is defined as a Class 1A risk factor for patients with chronic renal disease [27]. However, some studies noted increased HbA1c level for AKI following CABG is unclear (32). Additionally, the mortality rate of our patient group with AKI was determined to be severely increased in all groups.

6. CONCLUSION

This study showed that higher HbA1c levels have no effect in mortality rates after coronary bypass surgery of poorly controlled diabetic patients although the current risk calculator modules stated otherwise. However, the HbA1c levels have been found to be associated with the need for secondary intervention on long term postoperative period. This group of patients should be treated with aggressive medical therapy for blood glucose level regulation and long-term follow up is required during the postoperative period.

Acknowledgment

We did not receive any financial support for preparation of this article. We did not have communications with any company during the preparation of this article.

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How to cite this article: Aksoy R, Adademir T, Cevirme D, Yilmaz E, Sengor M, Koksal C, Rabus MB. The Effect of HbA1c Level on Gender-Specific Long-Term Morbidity and Mortality After Isolated Coronary Bypass in Poorly Controlled Diabetic Patients. Clin Exp Health Sci 2021; 11: 34-41. DOI: 10.33808/clinexphealthsci.782816