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Predictors of Mortality in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Objective: Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation (DECAF) score is considered a better predictor of mortality than other predictive tools. Mortality models are fitted to determine the better mortality prediction in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) having a DECAF score of 1-6 and ≥4 within 7 days of hospital admission keeping actual mortality as the gold standard. The data is collected from Chest Department, Fauji Foundation Hospital, Rawalpindi, Pakistan; from 15 May 2017 to 15 Nov. 2020

Methods: 146 Patients with COPD were selected from the emergency and OPD of Fauji Foundation Hospital Rawalpindi, Pakistan. The procedure began after the patients gave informed consent. Clinical features were documented, and investigations were carried out. The hospital administration, not the patient, was responsible for the expense of all the tests. A specially designed questionnaire was used for data collection.

Results: 146 patients were included according to the study's inclusion criteria. The mean age (years) of patients is 64.90+0.93. Patients with DECAF scores of 1 to 3 are 64%, the cases with DECAF scores of 4 are 26.7%, and those with DECAF scores of 5 and 6 are 8.9%. The two fitted binary logistic regression models indicate that among the independent variables DECAF score and duration of smoking significantly contribute to mortality. The accuracy of the fitted model is 96.6% and 90.2% respectively and the values of sensitivity, specificity, and positive and negative predictive values (i.e. PPV and NPV) are found to be appropriate for the fitted model.

Conclusions: The study concludes that DECAF score and duration of smoking affect the mortality in patients admitted with acute exacerbation of COPD. Patients admitted to hospitals with high DECAF scores and with more years of smoking should be admitted to the intensive care unit because they may require invasive ventilation due to respiratory failure and high mortality

Keywords: Mortality, Risk ratios, Modelling.

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Introduction

Chronic obstructive pulmonary disease (COPD) is among one of the major causes of morbidity and mortality worldwide.[4,5] COPD has a significant economic and social burden on the communities. It is more common in older people. The prevalence of COPD varies from 0.2%-37%.[2] About 3 million people died of COPD during the previous year comprising 6% of all deaths worldwide.[5]
COPD has a progressive course of disease that is worsened by exacerbations that affect the quality of life and increase both short and long-term mortality.[1,3] Acute exacerbations in this illness are responsible for 1 in 8 hospital admissions and about 4.4 to 7.7% in-hospital deaths.[7,8]
In the case of stable COPD, the BODE Index (Body mass index (B), Airflow Obstruction (O), Dyspnea (D), and Exercise capacity index (E)) has been validated as a satisfactory tool for predicting mortality. However, in the case of acute exacerbations, to date, few tools are available that predict mortality in hospitalized patients.

By identifying the risk factors for mortality, the level of care can be modified and decisions about early hospital discharge can be made avoiding wastage of resources.[6]

One of the few tools explored in the recent past in patients with exacerbations is the DECAF (Dyspnoea, Eosinopenia, Consolidation, Academia, Atrial Fibrillation) score. In some recent studies,[13,14]

It is found that a 0 score has in-hospital mortality of 0.5%, a score of 1 has 2.1%, a score of 2 has 8.4%, a score of 3 has 24%, a score of 4 has 45.6% and a score of 5 has 70% in-hospital mortality.[15] They took 107 patients having COPD, they used binary logistic regression to analyse the data and concluded that exacerbations of COPD are highly influenced by different factors such as the use of antibiotics, breathlessness, and history of ICS use. The sensitivity of score 1 is 0.99 which is the highest among the DECAF scores followed by a DECAF score of 2 which has a sensitivity of 0.93, a score of 4 has a sensitivity of 42% and a score of 5 has lowest sensitivity that is 0.15. Similarly, the specificity for the DECAF score of 5 is 0.99 which is the highest followed by a score of 4 which has a specificity of 0.96 and a score of 1 has a specificity of 0.24.[16]

The DECAF score is a new tool that needs further exploration in terms of reliability and validity. The DECAF Score shows promise for the risk stratification of patients hospitalized with acute exacerbation of COPD (AECOPD).[8] Studies in the past suggest DECAF score is a better predictor of mortality than the CURB-65 score, COPD and Asthma Physiology Score predictive tools.[9] The death rates for each grade of the DECAF Score suggest the following risk categories: DECAF 0-1 (‘low risk’; in-hospital mortality 1.4%); DECAF 2 (‘moderate risk’; mortality 8.4%); and DECAF 3-6 (‘high risk’; mortality 34.6%). About more than half of the patients hospitalized with AECOPD can be classified as low risk of both in-hospital and 30-day mortality and might therefore potentially be suitable for early discharge.[10]

It will enhance the knowledge of medical practitioners and policymakers for planning to take proper measures for referring patients with high DECAF scores and predicting mortality.

Materials and Methods

A cross-sectional validation study was conducted at the chest Department of Fauji Foundation Hospital Rawalpindi Pakistan. The duration of the study was from May 15, 2017, to Nov 15, 2020. Consecutive (non-probability) sampling was used for data collection.

Patients aged ranging from 40-90 years only have females including the tobacco smokers. Admitted patients to the hospital with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) were included in the study.

Diagnosed patients of respiratory diseases other than COPD. Asthmatic, Allergic rhinitis, Malignant disease, Severe pulmonary tuberculosis, Heart failure, Domiciliary oxygen, Pulmonary hypertension, and Obstructive sleep apnoea, were excluded from the study.

After approval from the ethical committee and informed consent, patients visiting the emergency department of Fauji Foundation Hospital with acute exacerbation of COPD were selected and those meeting the inclusion criteria were included in the study. They were evaluated in detail using history, general and systemic examination and parameters like hospital number, age, gender, eosinophil count, ABGs for pH, and ECG and chest x-ray. These patients were then followed during admission for mortality during 7 days of admission. The important variables measured are mortality, age, duration of smoking, BMI, Cerebrovascular Accident (CVA), DECAF score, Hypertension, and diabetes. Note that there are two types of variables in the study i.e., numerical, and categorical.

The DECAF score was calculated in patients with acute exacerbation of chronic obstructive pulmonary disease within 7 days of hospital admission along with other related variables so that we could do risk stratification at admission and modify our management according to the score. This score is feasible at the bedside because these parameters are usually measured on routine admissions.

The data about DECAF score, numerical and categorical variables were subjected to descriptive statistics, tests of association and two mortality models using binary logistic regression Data, The data were entered and analyzed in SPSS using version 22.0. The total number of patients included according to the inclusion criterion of the study was 146.

Associations are worked out using chi-square tests and different risk ratios for measured variables. Two binary logistic regression models are fitted to determine the best predictors of mortality in patients with acute exacerbation of chronic obstructive pulmonary disease one with having DECAF score of 1-6 and the other with a DECAF score of ≥ 4 within 7 days of hospital admission keeping actual mortality as gold standard.

For binary logistic regression, the dependent variable is mortality and the independent variables are age, duration of smoking, BMI, CVA, DECAF score, Hypertension, and diabetes. The following analysis of data has been done for these variables.

For the numerical variables, descriptive statistics is calculated whereas for the categorical variables, frequency distribution for each variable is done.

The Association between different variables and risk ratios have been worked out.

Logistic regression of mortality versus independent variables for all cases with DECAF scores 1-6 has been done.

Logistic regression of mortality versus independent variables for data with DECAF score of 1-6 and others with DECAF score of also sensitivity, specificity and model diagnostic accuracy the model has been worked out.

Results

For each numerical variable descriptive statistics and each categorical variable, frequency distribution is calculated and is given in Table 1.

Table 1: Descriptive statistics and Frequency distribution of variables

Variable	Mean ± SE		
Age	64.93 ± .937		
Duration_smoking	27.84 ± .935		
BMI	23.54 ± .336		
DECAF_score	3.15 ± .086		
Variable		**Frequency**	**Percentage**
Hypertension			
No		33	22.6
Yes		113	77.4
Diabetes			
No		92	63.0
Yes		54	37.0
DECAF Score			
1.00		4	2.7
2.00		38	26.0
3.00		52	35.6
4.00		39	26.7
5.00		10	6.8
6.00		3	2.1
CVA			
No		136	93.2
Yes		10	6.8
Mortality			
Alive		136	93.2
Dead		10	6.8
Total		146	100.0

Among 146 patients in the study, the age ranged between 40 and 93 years with a mean of 64.93 and a standard error of 0.937. The duration of smoking was between 2 and 50. The minimum smoking period of two years may be attributed to their previous history of wood burning. The BMI ranged from 16 to 39 and the DECAF score was between 1 and 6.
Table 1 indicates that most of the patients i.e. 77 % have hypertension, only 37% have diabetes and only 7% of the cases have CVA. The patients with DECAF score of 1,2,3 (2.7+26+35.6 =64.3) are 64 %. The cases with DECAF scores of 4 are 26.7% and the cases with DECAF scores of 5 and 6 are 8.9%. Also, about mortality 93% are still alive and only 7% have died.

The association between DECAF score versus mortality, and CVA versus mortality has been worked out and is given in Table 2a.

Table 2a: DECAF score versus mortality cross-tabulation and Chi-Square Tests

Variable		Mortality		Total	Died %	P Value
		alive	Dead			
DECAF score	1.00	4	0	4	0	<.0001
	2.00	38	0	38	0	
	3.00	52	0	52	0	
	4.00	36	3	39	8	
	5.00	5	5	10	50	
	6.00	1	2	3	66	
Total		136	10	146		

Table 2b: CVA versus mortality Cross tabulation and Chi-Square Tests

Variable		Mortality		Total	P-Value
		alive	dead		
CVA	No	127	9	136	0.683
	Yes	9	1	10	
Total		136	10	146	

From Table 2a, it is clear, that no patient died with a DECAF score of 1, 2 and 3. There are 39 patients with a DECAF score of 4 and 3 died i.e.,7.6% died whereas there are 10 patients with a DECAF score of 5 and 5 died i.e., 50% died and the number of patients with a DECAF score of 6 66.67%. There are (10+3=13) patients with a DECAF score of 5 and 6 and 7 of them died i.e. (53.8%) died. It can be concluded that as the DECAF score increases, the %age of patients who died, increases. The chi-square test value (52.964) gave the p-value = 0.00. The p-value = 0.00 means that results are significant indicating thereby that there is an association between DECAF score and mortality. It is concluded that DECAF score and mortality are related.

From Table 2b it is clear, that most of the patients without CVA are alive and only 10% of patients with CVA have died. As far as the association between CVA and mortality is concerned, the p = 0.52, which means that there is no association between CVA and mortality i.e., CVA and mortality are not related.

Two binary logistic regressions were performed using SPSS 22 to determine whether the mortality can be predicted from the DECAF score, CVA, diabetes, hypertension, BMI, Duration of smoking and age. The dependent variable is mortality (died, alive) and the independent variables are DECAF score, CVA, diabetes, hypertension, BMI, Duration of smoking and age. The following two cases have been evaluated.

i. Logistic regression of all variables and cases with DECAF score (1,2,3, 4,5,6)

ii. Logistic regression of all variables but cases with DECAF score ≥ 4

For case (i) where all DECAF score values (1,2,3, 4,5,6) are used with other independent variables, the SPSS output is given in Table 3a and Table 3b.

Table 3a gives a model summary; the Hosmer and Lemeshow test is used to test the hypothesis that the fitted model is correct, and the higher p-values indicate a better fit.

Table 3b gives the fitted binary regression model results.

Table 3 a,b: Model Summary and Logistic Regression of Mortality vs Independent Variables

Observed		Predicted		
		mortality		Percentage Correct
		alive	dead	
mortality	alive	135	1	99.3
	dead	4	6	60.0
Overall %				96.6

Table 3b: Logistic Regression of Mortality vs independent variables

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
DECAF score	2.978	.949	9.855	1	0.002	19.654	3.061	126.1
CVA(1)	1.355	2.353	.332	1	0.565	3.877	0.039	390.1
diabetes			0.001	2	0.999			
diabetes(1)	13.472	40192.9	0.000	1	1.000	709489 .8	0.001	.
diabetes(2)	13.432	40192.9	0.000	1	1.000	681552 .6	0.001	.
hypertension	18.759	51.799	0.000	1	0.997	5.625	0.001	.
BMI	.073	0.104	.504	1	0.478	1.076	0.879	1.3
duration_smoking	.128	0.071	3.290	1	0.070	1.137	0.990	1.3
age	-.074	0.069	1.146	1	0.284	0.928	0.810	1.0
Constant	-49.199	40527.3 05	.000	1	0.999	0.001		

The Nagelkerke R Square = 0.663 and Hosmer and Lemeshow test p-value = 0.996 (non-significant). These values are reasonably high as desired so the null hypothesis that the model is a good fit is not rejected. The model is a good fit and the predicted correct classification of the fitted model is 96.6%.

In Table 3b, the DECAF score has p-value = 0.002<0.01 which means a highly significant result statistically, the value for the duration of smoking = 0.07, which is significant at a 10% level of significance, the p-values for all other variables are not significant (all greater than 0.10). It means that only DECAF score and smoking contribute to mortality statistically and all other variables do not contribute based on the analysis of this data.

The cross Table 4(a) regarding DECAF score vs mortality indicates that the number of patients who died with DECAF scores of 1,2,3 is zero. Only the patients with a DECAF score of 4 or more died; so, to compare the DECAF score of 4 versus 5 and 6, only those cases are considered whose DECAF score is 4 or more. There are 51 such cases.

These results are using logistic regression on 51 cases where DECAF score is and are given in Table 4a and Table 4b.

Table 4a: Model Summary

Observed		Predicted		
		mortality		Percentage Correct
		alive	dead	
mortality	alive	40	1	97.6
	dead	4	6	60.0
Overall Percentage				90.2

Table 4 gives 90 % correct classification where the R Square = 0.558 and test p-value = 0.761 indicating that the model is a good fit.
The DECAF score has p value=0.007<0.01 which is highly significant statistically, the value for the duration of smoking=0.097, which is significant at a 10% level of significance, and the p values for all other variables are not significant (all greater than 0.10). It means that only DECAF score and smoking contribute to mortality statistically and all other variables do not contribute based on the analysis of this data. These results are the same as have been obtained with all the patients in Table 3b.
The sensitivity specificity and diagnostic accuracy are:
Sensitivity = 90.91; =; Specificity = 85.71; PPV= 97.5; NPV = 60 and DA = 0.92
The model gave reasonably high values of sensitivity = 90.91 and specificity = 85.71, PPV=97.5, NPV= 60 and DA=0.902. For the two fitted logistic models, the correct predicted percentage is 96.6 and 90.2 indicating that these models are appropriate in predicting the true status of the cases.

Table 4b: Logistic Regression for Mortality vs DECAF score ≤ 4

a. Variable	b. B	c. S.E.	d. Wald	df	Sig.	g. Exp(B)
h. age	i. -.06	j. .07	k. .894	1	m. .344	n. .935
duration_smok	p. .12	q. .07	r. 2.754	1	t. .097	u. 1.127
BMI	w. .07	x. .10	y. .534	1	aa. .465	bb. 1.078
hypertension	dd. 20.23	ee. 11.64	ff. .000	1	hh. .999	ii. 3.492
diabetes	kk. -.005	ll. 1.14	mm. .000	1	oo. .996	pp. .995
CVA	rr. -1.30	ss. 2.20	tt. .348	1	vv. .555	ww. .272
DECAF score	yy. 2.74	zz. 1.02	aaa. 7.166	1	ccc. .007	ddd. 15.537
Constant	fff. -34.95	ggg. 11551.64	hhh. .000	1	jjj. .998	kkk. .000

Discussion

Chronic obstructive pulmonary disease (COPD) is among one of the major causes of morbidity and mortality worldwide and has a significant economic and social burden on the communities.[2] The DECAF score is a rather new tool being used as a predictor of mortality.[1] The DECAF Score shows promise for the risk stratification of patients hospitalized with acute exacerbation of COPD (AECOPD).[5] It needs further exploration in terms of reliability and validity. In this study, we have used the DECAF score along with other predictors of mortality in patients hospitalized with acute exacerbation of COPD (AECOPD).
The results of this study showed that DECAF score and mortality are associated whereas CVA and mortality are not associated. Similar results have been obtained by Yang IA, Jenkins CR, Salvi SS.[3]
Binary logistic model fitting results in the study indicate that the significant predictors of mortality are DECAF score and smoking. These results are in agreement with,[11,12] but these fitted models have better accuracy. Age was not a significant factor as observed

in the fitted model but this finding is not in agreement with Chow R, et. al's study.[8] An interesting result in fitting the two binary logistic regression models is that the models resulted in the same significant predictors of mortality and the same model accuracy. The major limitation of this study is that the patients included are only females. It is because the sample is taken from the Fauji Foundation hospital which is exclusively meant for families of x-servicemen. In this study, mortality was checked only within 7 days of hospital admission and the variables included are mortality, age, duration of smoking, BMI, Cerebrovascular Accident (CVA), DECAF score, Hypertension, and diabetes. More hospital-based and socio-economic variables can be included in the study that may help to warn the patients at home to seek urgent medical help.

For further research, the study may include both male and female patients. The separate binary logistic models for males and females may compare their parameters and a full model may also be fitted to compare their model adequacy. Further research is also required to assess the mortality of patients beyond 7 days and up to 30 days after exacerbation

Conclusion

From the data analysis using the association between measured variables, risk ratios and logistic regression fitted models with its diagnostic accuracy, it is concluded that DECAF score and duration of smoking affect the mortality in patients admitted with acute exacerbation of COPD. It is recommended that Patients admitted to hospitals with high DECAF scores and with more years of smoking should be admitted to the intensive care unit because they may require invasive ventilation due to respiratory failure and high mortality.

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