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# Adverse Drug Reactions after the use of Benznidazole in Bolivian Patients with Chagas Disease



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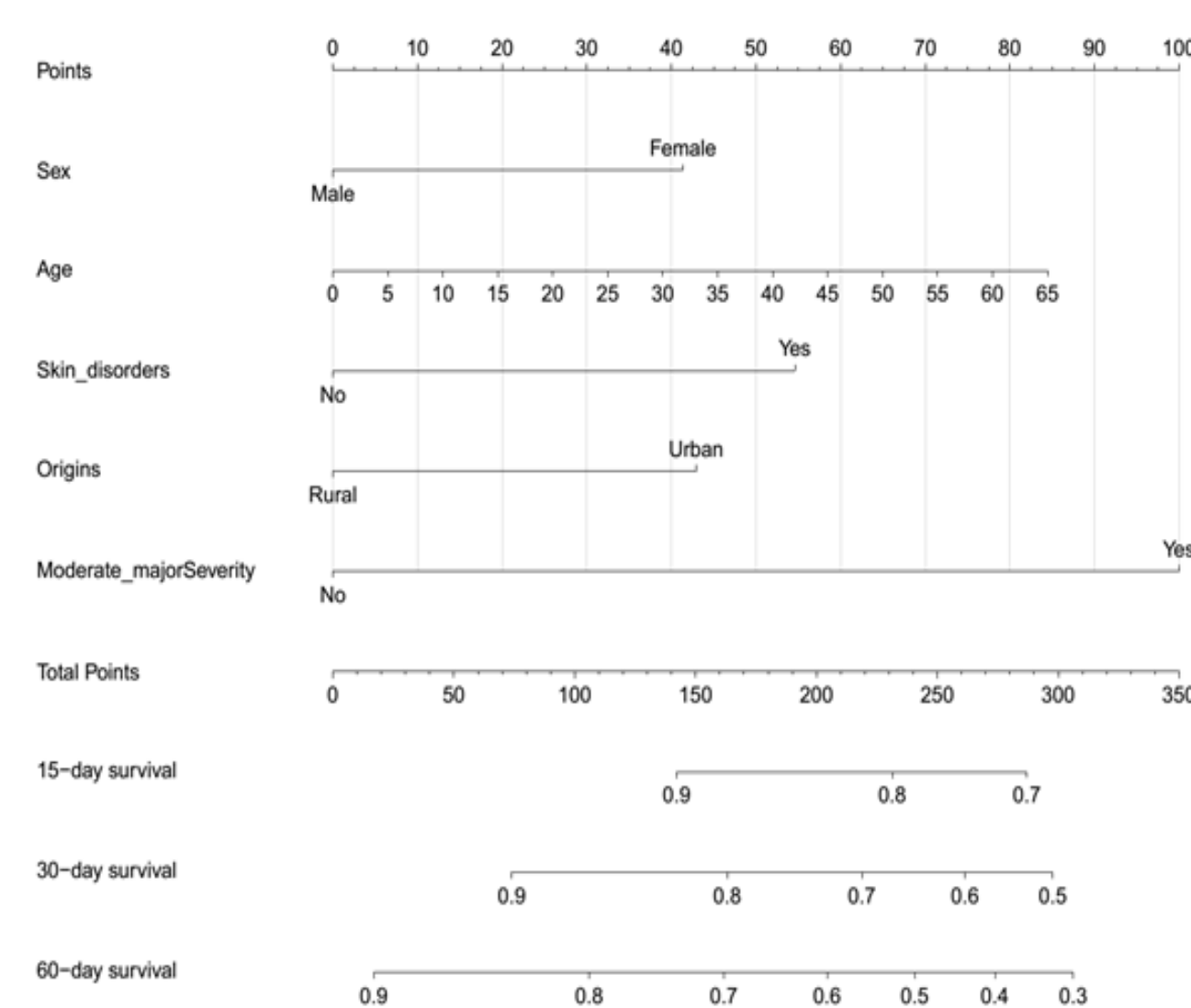
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## Background

Chagas disease remains an important problem in the world and there is an estimate of more than 10 million infected people worldwide. Benznidazole (BZN) is the main drug used for etiologic treatment of this disease. However, about 17 to 31% of patient discontinued the BZN treatment.

## Methods

In the present study, 2833 patients were treated with BZN provided 2 or 3 times per day for about 60 days at 5-7.5 mg/kg-day (maximum 300 mg/day) from 2009 to 2012. The statistical analysis was performed with epicalc, Hmisc and rms packages (R software). The multivariate Cox regression model was developed to evaluate the predictors of BZN treatment discontinuation.



Nomogram to calculate predicted 15-days, 30-days and 60-days survival (probability of complete BZN treatment).

## Aim

The aim of the present study was understand the predictors of BZN treatment discontinuation over time.

## Results

Definitive treatment discontinuation was observed in 520 (21.8%) patients and five predictors were identified, the median time to treatment discontinuation was 23 days (median 23.10± 8.42 days). BZN treatment discontinuation was significantly increased in female patients (adjusted HR= 1.42), according to age (adjusted HR= 1.23 per added year), patients who lived in urban areas (adjusted HR=1.44), patients who had had severe or moderate adverse drug reactions - ADRs (adjusted HR=2.32) and patients who had had skin reactions (adjusted HR=1.58).

ADR					
VARIABLE	CATEGORY	YES,n(%)	NO,n(%)	P-value	Total,n(%)
Sex	Male	500(25.9)	1453(74.1)	<0.001	1953(68.5)
	Female	220(36.5)	381(63.5)		601(21.5)
Age median(IQR)		41(31.46)	37(27.47)	<0.001	78(2.8)
Age group	1 to 12 years	51(9.2)	79(10.6)	<0.001	130(4.6)
	13 to 21 years	44(14.4)	118(38.4)		162(5.7)
	22 to 35 years	104(25.4)	187(44.5)		291(10.3)
	> 35 years	112(38.1)	161(51.9)		273(9.6)
	All ages	211(37.1)	345(52.9)		556(19.5)
Town	Urban	134(25.3)	366(64.7)	0.004	500(17.6)
	Rural	265(37.7)	415(62.3)		680(24.0)
Origin	Rural	109(25.9)	311(54.1)	0.005	420(14.8)
	Urban	102(34.6)	154(50.4)		256(9.0)
Treatment duration median(IQR)		42(30.8)	41(30.4)	0.004	83(2.9)
TLV baseline	Normal	351(58.2)	533(91.8)	0.003	884(31.0)
	No normal	167(35.2)	262(44.8)		429(15.1)
Cardiac symptoms	No	128(19.3)	107(40.6)	0.001	235(8.3)
	Yes	131(54.8)	111(45.2)		242(8.5)
Digestive symptoms	No	125(44.1)	160(55.9)	0.006	285(10.1)
	Yes	151(31.8)	317(68.2)		468(16.5)
Treatment	Complete	215(36.0)	668(73.0)	0.001	883(30.9)
	Complete	285(45.2)	339(54.8)		624(21.9)
Total		1291(54.1)	1094(45.9)		2385(84.0)

Variables associated to ADRs in treatment with BZN in Chagas disease Patients (N=2383). \*Data available for 1913 patients.

Multivariate Cox Regression			
Variables	Reference	HR (95% CI) <sup>a</sup>	P-value
Sex	Female	1.42 (1.19 - 1.69)	0.0001
	Male**		
Age, years		1.23 (1.08 - 1.40)	0.0018
Origins	Urban	1.44 (1.15 - 1.79)	0.0015
	Rural**		
Moderate-major Severity	Yes	2.32 (1.87-2.87)	<0.0001
	No**		
Skin disorders	Yes	1.58 (1.31-1.92)	<0.0001
	No**		
Predictive accuracy, %		65.6	

\*P-value <0.05, \*\* Reference category. Note: HR=Hazard Ratio. a Adjusted HRs were calculated by multiple Cox regression model. b Regression coefficient

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## Conclusion

Female sex, older patients, those who lived in urban areas, patients who had had moderate or severe ADRs and those who had had skin disorders had a higher risk for BZN treatment discontinuation. For these patients, a close follow-up should be carried out, at regular intervals of at least once a week to monitor BZN treatment.

**Impact of study:** The results of this study may help on identification of patients at high risk for BZN treatment discontinuation. Also, these results suggest that a close follow-up by health professionals could be necessary in order to improve adherence and early detection of ADRs.

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