Risk of Chronic Cardiomyopathy Development and its Determinants in Patients with the Acute Phase and Indeterminate Form of Chagas Disease: A Systematic Review and Meta-Analysis

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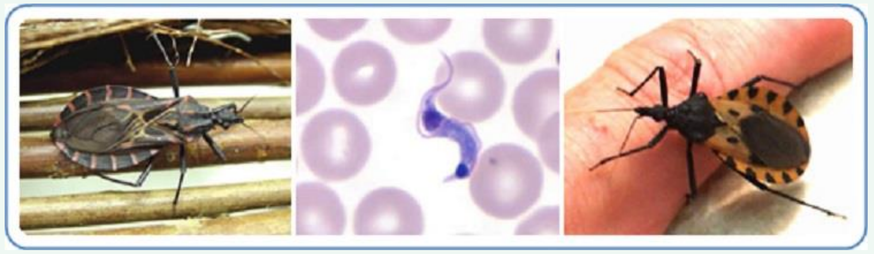


Figure 1 : Left And Right: Various Species Of Triatomine Bugs, Which If Infected Can Transmit *T. Cruzi*. Center: *T. Cruzi* trypomastigote In A Thin Blood Smear Stained With Giemsa.

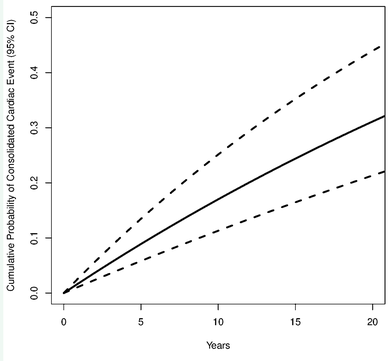
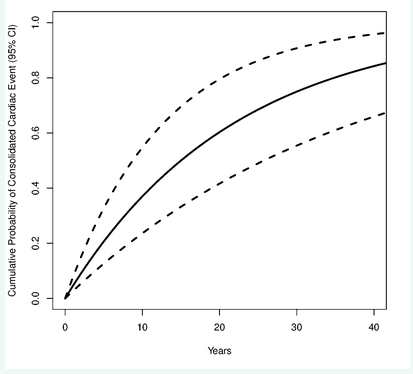


Figure 2: Cumulative risk of a cardiac event for studies with the indeterminate form of Chagas disease

Figure 3: Cumulative risk of a cardiac event for studies with the acute form of Chagas disease



Background

- Chagas cardiomyopathy, a complication of Chagas disease occurs in 20-30% of untreated cases, causing substantial morbidity and mortality
- Presently, we lack precise annual estimates of the risk of cardiomyopathy development among patients with the acute and indeterminate forms of Chagas disease

Methods

- Design: Systematic review and meta-analysis
- Timeline: January 1945 to October 2018
- Population: Longitudinal observations of individuals with acute or indeterminate form until the development of cardiomyopathy
- Data Source: MEDLINE, Web of Science Core Collection, Embase, Cochrane Library, and LILACS
- Studies critical appraisals were performed utilizing the JBI Reviewer's Manual checklists, and data was collected from published studies
- Events were defined as the composite of development of any new arrhythmias or ECG changes, echocardiographic changes including dilated cardiomyopathy or segmental wall motion abnormalities, and sudden cardiac death
- We used random-effects meta-analysis in STATA software to obtain pooled estimated annual rates.

Table 1. Baseline characteristics and clinical outcomes of indeterminate staged patients

First Author (study onset)	Study Design	Country	Cases	Man (%, (n))	Age	Intervention*	Study Duration (years)	Cardiac Events Rate† (%, (n))	Rate Estimate‡	95% CI	% Weight
Viotti et al (1984)[18]	Cross-sectional	Argentina	505	65·9 (333)	40·5	No	9·9	27.5% (139)	3.3	2.8-3.8	4.9
Machado et al (1997)[19]	Prospective Cohort	Brazil	23	34·8 (8)	26·7	Benznidazole therapy	13	17.4% (4)	1.5	0.6-3.9	4
Zulantay et al (1992)[20]	Prospective Cohort	Chile	10	..	..	Other antiparasitic therapy¶	7	10% (1)	1.5	0.2-10.7	2.5
Mota et al (1974)[21]	Prospective Cohort	Brazil	248	43·5 (108)	..	No	5·8	36.3% (90)	7.8	6.3-9.6	4.9
Coura et al (1974)[22]	Prospective Cohort	Brazil	60	..	..	No	10	38.3% (23)	4.8	3.2-7.3	4.7
Pereira et al (1977)[23]	Case control	Brazil	77	..	31·2	No	6	42.9% (33)	9.3	6.6-13.2	4.8
Espinosa et al (1973)[24]	Prospective Cohort	Venezuela	18	50 (9)	37	No	9·4	5.5% (1)	0.6	0.1-4.3	2.5
Apt et al (1992)[25]	Randomized Clinic. Trial	Chile	202	..	..	Other antiparasitic therapy¶	9	14.9% (30)	0.2	0.1-0.6	4.1
Fabbro et al (1970)[26]	Prospective Cohort	Argentina	179	..	..	Benznidazole or Nifurtimox|	14	5.6% (10)	0.4	0.2-0.8	4.5
Colantonio et al (1995)[27]	Retrospective Cohort	Argentina	86	..	10	Benznidazole or placebo|	13	18.6% (16)	1.6	1-2.6	4.7
De Andrade et al (1991)[28]	Prospective Cohort	Brazil	125	..	10·4	No	3	4% (5)	1.4	0.6-3.3	4.1
Andrade et al (2005)[29]	Prospective Cohort	Brazil	9	..	..	Benznidazole therapy	5	22.2% (2)	5	1.3-20.2	3.3
Fragata-Filho et al (2002)[30]	Prospective Cohort	Brazil	310	34·5 (107)	34·5	Benznidazole therapy**	18	25.8% (80)	1.7	1.3-2.1	4.9
Pereira et al (1985)[31]	Prospective Cohort	Brazil	92	..	39·6	No	4·5	13% (12)	3.1	1.8-5.5	4.6
Viotti et al (1990)[32]	Prospective Cohort	Argentina	731	48·6 (355)	43·7	No	8	4.7% (34)	0.6	0.4-0.8	4.8
Ianni et al (1998)[33]	Prospective Cohort	Brazil	160	38·8 (62)	36·5	No	8·2	2.5% (4)	0.3	0.1-0.8	4
Da Silva et al (1994)[34]	Prospective Cohort	Brazil	73	..	..	No	7·8	11% (8)	1.5	0.7-3	4.4
Castro et al (1975)[35]	Prospective Cohort	Brazil	120	..	..	No	13	15.8% (19)	1.3	0.8-2.1	4.7
Macedo (1976)[36]	Prospective Cohort	Brazil	471	..	..	No	5	40.3% (190)	10.3	8.9-11.9	4.9
Manzullo et al (1970)[37]	Prospective Cohort	Multicenter§	3336	58·3 (1944)	..	No	3	23.1% (771)	8.8	8.2-9.4	5
Storino (1985)[38]	Prospective Cohort	Argentina	78	44·9 (35)	36·1	No	5	20.5% (16)	4.6	2.8-7.5	4.7
Brasil (1960)[39]	Prospective Cohort	Brazil	43	..	..	No	9·1	18.6% (8)	2.3	1.1-4.5	4.4
Forsichon (1975)[40]	Prospective Cohort	Brazil	885	42·2 (373)	..	No	10	3.6% (32)	0.4	0.3-0.5	4.8

*Antiparasitic treatment. †Cardiac outcomes include development of any new electrocardiograph (ECG) changes, echocardiograph changes, arrhythmias, dilated cardiomyopathy, segmental motion abnormality, or mortality related to Chagas disease. ‡Rate estimate was calculated based on exponential survival method (1/years *-log (100-cardiac events/total cases); §Argentina, Bolivia, Brazil, Chile, Paraguay, Uruguay, Peru. ¶ Allopurinol and itraconazole. | 2 cardiac events from 63 subjects on treatment arm, and 8 events from 116 subjects on untreated arm. | 8 cardiac events from 48 subjects on treatment arm, and 8 events from 38 subjects on untreated arm. **55 cardiac events from 263 subjects on treatment arm, and 25 events from 47 subjects on untreated arm

Table 2. Baseline characteristics and clinical outcomes of acute staged patients.

First Author	Study Design	Country	Type of Transmission	Cases	Man (%, (n))	Age	Study Duration (years)	Cardiac Events Rate* (%, (n))	Rate Estimate†	95% CI	% Weight
Pedrosa et al (1966)[41]	Case series	Brazil	Vector	40	57·1 (24)	..	9	35·0% (14)	4.8	2.8-8.1	11.6
Inglessis (1989)[42]	Case series	Venezuela	Vector	10	60 (6)	23	5·5	60.0% (6)	16.8	7.3-38.4	10.7
Bastos et al (2006)[12]	Case series	Brazil	Oral	11	61·5 (8)	24·6	0·5	54·5% (6)	157.5	69.1-359.3	10.7
Pinto et al (1992)[43]	Prospective Cohort	Brazil	Oral	179	..	..	5·5	29·1% (52)	6.1	4.7-8.1	12.1
Gus et al (1965)[44]	Case series	Brazil	Oral	17	47·1 (8)	30·4	26	35·3% (6)	1.7	0.7-3.8	10.7
Urrutia (1972)[45]	Case series	El Salvador	Vector	40	35 (14)	..	5	15.0% (6)	3.3	1.5-7.2	10.7
Ortiz et al (2007)[46]	Prospective Cohort	Brazil	Oral	25	..	..	1·3	16·0% (4)	13.5	5.1-36.1	10.1
Laranja et al (1956)[47]	Prospective Cohort	Brazil	Vector	40	..	..	10	42·5% (17)	5.5	3.4-9.0	11.7
Dias (1940)[48]	Prospective Cohort	Brazil	Vector	59	..	..	27	30·5% (18)	1.3	0.8-2.1	11.7

*Cardiac outcomes include development of any new ECG changes, echocardiograph changes, arrhythmias, or sudden death. † Rate estimate was calculated based on exponential survival method (1/years *-log (100-cardiac events/total cases)

Results

- 10,761 records were identified through database searches of which 5,005 studies were screened for eligibility
  - 298 full-text articles were reviewed, and 187 studies were included in the final synthesis for appraisal
- Twenty-three studies had longitudinal observation outcomes for the chronic indeterminate form of Chagas disease and nine for acute Chagas infection
- Pooled annual rate estimate of cardiomyopathy of 1 · 9% per year (95% CI: 1·3 - 3·0%, I^2 =98·0%, τ^2 (ln scale) = 0·9992) per year in chronic indeterminate Chagas patients
- Pooled annual rate estimate of cardiomyopathy of 4 · 6% (95% CI: 2·7 - 7·9 %, I^2 =86·6%, τ^2 (ln scale) = 0·4946) per year in acute chagasic patients.

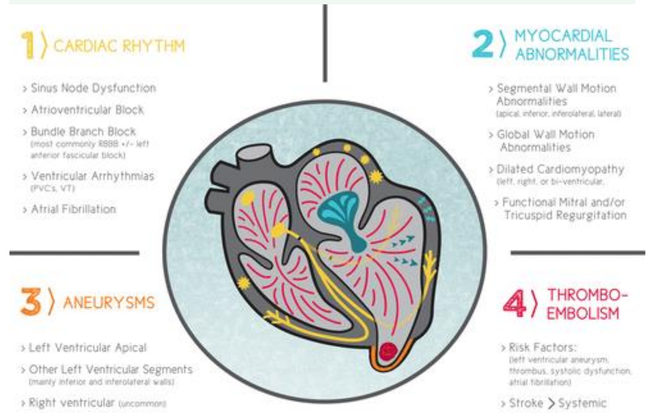


Figure 4: Illustration of the most common findings in patients with Chagas cardiomyopathy

Conclusion

- People living with the indeterminate form of chronic Chagas disease have a significant annual risk of cardiomyopathy development
- This risk more than doubles for patients diagnosed with acute infection.

References

- CDC DPDx, 2019. *Left And Right: Various Species Of Triatomine Bugs, Which If Infected Can Transmit T. Cruzi. Center: T. Cruzi Trypomastigote In A Thin Blood Smear Stained With Giemsa*. [image] Available at: <https://www.cdc.gov/parasites/chagas/> [Accessed 30 March 2020].
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