Infarct Combat Project

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Effects of the Cardiotonic + Coronary Dilator in the Infarcting Clinical Picture

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Summary

Disclosure of the Myogenic Theory of myocardial infarction which advocates the Regional Myocardial Insufficiency, spontaneously irreversible, as the pathophysiologic mechanism of Infarcting Clinical Picture that, abandoned to its fate, evolves to the acute myocardial infarction, primary, and coronary thrombosis, secondary, not obligatory.

As consequence, the administration of cardiotonic + coronary dilator represents the natural imposition and its effects should serve to strengthen the Myogenic Theory precepts in opposition of the classic concepts of the Thrombogenic Theory of myocardial infarction.

Introduction

In this paper we present our clinical experience in acute cases of myocardial infarction which we prefer to recognize, at first, as having infarcting clinical picture (ICP) – evolving to the myocardial infarction, treated according to the precepts of the Myogenic Theory, developed by us in 1972, with the exclusive use of the association of the cardiotonic + coronary dilator calcium antagonist, as therapeutic attack, followed by an uninterrupted maintenance therapy (1-12).

Regarding the pathophysiology of the I stage of ischemic coronary- cardiomyopathy, there is general consensus in the identification of stable angina as triggered by physical exertion or emotions. Meanwhile, the II and III stages, characterized by unstable angina and myocardial infarction, w/out Q-wave and with Q-wave, as phases of the same process, gradual and progressive, have been differently considered by orthodox cardiologists, followers of the Thrombogenic Theory, who admit the pathophysiology as resulting from primary thrombotic process.

We advocate the myocardial process as primary, starting from declared regional insufficiency, episodic and spontaneously reversible in unstable angina and made irreversible in the infarcting clinical picture, evolving to the acute myocardial infarction.

Meanwhile, the orthodox cardiology, despite the unsuccessful clinical experience carried out in all countries with the use of oral anticoagulants and the parenteral Heparin in the prevention and treatment of myocardial infarction during 25 years (1944-69), still advocate the coronary vasospasm and / or primary coronary thrombosis as the pathophysiological mechanism in these stages.

Recently, the orthodox cardiology returned to experiment this therapy with anticoagulants, admittedly unsuccessful, in isolation, as preventive or in continuation to the thrombolytic therapy, in disagreement with the records of the 60s. Therefore, in recent memory and very much alive in the minds of those who participated of their use which very early found the failure of these drugs.

As proponents of the Myogenic Theory of myocardial infarction, we advocate the installation of regional myocardial insufficiency, spontaneously, in myocardial segment severely compromised, triggering absolute myocardial ischemia, spontaneously irreversible, becoming the infarcting clinical picture that, left to his fate, inevitably evolves to the installation of acute myocardial infarction - considered as primary process – conditioning the coronary thrombosis, secondary and not obligatory (Table 1).

Table 1

Ischemic Coronary-Cardiomyopathy

Pathophysiology of Infarcting Clinical Picture

1 – Regional Myocardial Insufficiency, Primary
(Regional circulatory stagnation, platelet aggregates.
Possible vasospasm in situ or remotely. Increased volumes and residual
Systolic and diastolic pressures and in pulmonary capillary pressure. Decreased
ejection fraction and ejection of left ventricular phase. Increased parietal tension
and stroke volume)

2 - Regional Myocardial Ischemia, Secondary

3 – Infarcting Clinical Picture evolving to:

Primary Myocardial Necrosis (Infarction)

↓

Secondary Coronary Thrombosis, Not Obligatory

In practice, the coronary thrombosis that has been presented by the orthodoxy as primary process has often not been found in cases of acute myocardial infarction, as shown on the records of angiographically normal or pervious coronary arteries.

Interestingly, recent papers (15-20) using precocious coronary angiographies in acute myocardial infarction, or better, yet in infarcting clinical picture have shown complete coronary occlusion in 41-75% of cases of myocardial infarction with Q-wave and in 26-46% of cases of myocardial infarction without Q-wave. Moreover, in the myocardial infarction without Q-wave, has occurred increased incidence of total coronary obstruction, according the time elapsed since the beginning of the crisis / coronary angiography (26% within the first 24 hours and 42% within 72 hours - 7 days) and

reduction in the process of subtotal obstruction with the increase of the referred interval (34% within the first 24 hours, and 18% within 72 hours - 7 days).

These data should deserve reflection, by coinciding with old pathological records made public since 1956 (21-43), wondering:

"Coronary thrombosis: cause or consequence of myocardial infarction?"

In particular, the experiment from Hellstrom (43) was also very incisive with the record of thrombosis in normal coronary artery, secondary to acute myocardial infarction, caused by coronary artery ligature and, some time after, its release.

Necessarily, it must be admitted that for different pathophysiological mechanisms should be also used diverse or specific therapeutic methods, for each model hypothesized.

Casuistry and Method

It presents part of the casuistry of infarcting picture exclusively under medical treatment, according to the Myogenic Theory precepts, represented by 1109 patients, being 918 pts (82.7%) males and 191 pts (17.3%) females, with mean ages, respectively, of 56 years (26-86 years) and 62 years (32-89 years), and globally registered as ages of <70 years (956 pts: 86.2%) and > 70 years (153 pts: 13. 8%).

The crisis / hospitalization interval indicated the average of eight hours in 1109 pts (< 6h in 586 pts and > 6h in 523 pts.)

The electrocardiographic control was represented by continuous monitoring for 24-48h, supplemented by the daily record of 13 derivations (D1, D2, D3, aVR, aVL, V4R, V1-V6) and in the last year of observation were also recorded V6R and V5R derivations, in consequence of the manifested importance and absolute necessity of early recognition of the association of the infarctions of right and left ventricles, or from isolated processes.

The identification of electrocardiographic cases was performed according to our new and simplified ECG classification of acute myocardial infarction (13,14), characterized by three different types of myocardial infarction:

1. Left ventricle infarction, isolated: in 61.8% of the cases, with pattern of inferior wall infarction and in 68% of cases with pattern of anterior wall.
2. Right ventricle infarction, isolated or associated to unapparent left ventricle infarction: only registered in infarction pattern of inferior wall + primary alterations of infarction in derivations V4R, V5R e V6R; representing 15.1% of cases with pattern of inferior wall and 8% of the casuistry.
3. Association of left ventricle and right ventricle infarctions: in 38.2% of cases of myocardial infarction, with pattern of inferior wall and in 32% of cases, with pattern of anterior wall.

The serial enzymatic reactions - SGOT, LDH, CPK, and CK-MB - were held at first every 12 hours and from the third year every 24 hours, for 6 days.

The therapeutic routine recommended by the Myogenic Theory for the infarcting clinical picture is characterized by the association of cardiotonic + coronary dilator (Intravenous), as therapeutic attack during 6 days. This is followed by maintenance treatment with the association of cardiotonic + coronary dilator (Oral Route) when the cases are recognized as having its restored myocardial and symptomatic stability and thus continuously treated (Table 2).

Table 2

Terapeutic Attack in Infarcting Clinical Picture

Cardiotonics:

Strophanthin-K:	0,25-0,34 mg/day, IV
Strophanthin-G:	0,25-0,50 mg/day, IV
Lanatoside-C:	0,40 mg/day, IV
Digoxin:	0,50 mg/day, IV

Coronary Dilators

Dypiridamole:	20 mg/day, IV
Verapamil:	240 mg/day, OR
Prenylamine:	180 mg/day, OR
Nifedipine:	30 mg/day, OR

IV: Intravenous OR: Oral Route

The strophanthin K or G was used in 962 pts. and digitalis in 147 pts. in the first phase of treatment.

Results

The use of the association of cardiotonic + coronary dilator in infarcting clinical picture, since the beginning were recorded major transformations in the clinical evolution of the cases, never seen before, in such a short space of time (5 - 10 days of hospitalization), and with no deleterious effects.

In the infarcting clinical picture, for the first time, was used as cardiotonic, elective and preferably, the strophanthin-K or G (IV), by formal imposition of the pathophysiological mechanism, and not speculatively, as had happened in the past, but marked, always, with great enthusiasm for the results achieved in many therapeutic trials (44-51).

From very early on, with the use of the new therapeutic routine, we begin to register:

- Great responsiveness and absolute tolerance to the medication.
- Surprising reduction in the incidence of complications, commonly recorded in the early hours of the infarcting clinical picture (Table 3).
- Benefic effects on Tachyarrhythmias and on the course of cardiac arrests, at the time of admission.

The changes that occurred in the clinical evolution of the cases treated in this manner appeared to us to indicate that those admitted to the Coronary Units as having acute myocardial infarction, at the time of admission, yet were not infarcted. Therefore, we have denominated these cases, yet in evolving state, of infarcting clinical picture.

Evolution calmer and safer with clear changes in the behavior of the records in the precocious enzymatic peaks (24-48h) which were relatively lower. The great majority of cases of infarcting clinical picture (708 pts: 63.8%) shows enzymatic peaks <3xNormal and with exceptionally low mortality (7 pts: 0.9%), while the remainder (401 pts: 36.2%) presents enzymatic peaks >3xNormal

(around 5xN) and with higher mortality (129 pts: 32.1%); for an overall mortality recorded of 12.2% (139/1109 pts).

Cases with enzymatic peaks <3xNormal began to be called as having infarcting clinical picture - halted (ICP-H) and 20% of these, with enzymatic peaks within the normal or slightly increased, were considered as cases of myocardial infarction –avoided; The remaining cases with enzymatic peaks > 3xNormal, were regarded as cases of infarcting clinical picture -infarcted (ICP-I), but attenuated.

Such division of the cases in ICP-H and ICP-I, should serve as secure evidence of the unquestionable effects of restraining in the necrotic process, in most cases, through the correction of Regional Myocardial insufficiency and its ischemic and hemodynamic consequences, with the recovery of viable myocardial fibers, minimizing also the degrading effects on the myocardium and reducing the infarct size.

Analysis of the material studied, taking into account the relationship between the female and male Sex, the Ages < or > 70 years, crisis / hospitalization interval < or > 6 hours and enzymatic peak values responsible for the significant division of ICP-H and ICP-I, we verified that the mortality has been shown prevalent in Females in Age > 70 years, in the crisis / hospitalization interval > 6h and significantly in the group ICP-I.

Analytical study of the cases labeled as ICP-H and ICP-I and the specific confrontation between the many prognostic factors pointed out, we got clear evidence on the beneficial effects of the new therapeutic routine, with the association of cardiotonic + coronary dilator on Morbidity and Mortality (Tables 3, 4, 5, 6).

Table 3

Acute Myocardial Infarction

Índices of Clinical Complications and Mortality According to Age

Complications	1290 cases	Mortality		Total
		<70 years	>70 years	
	%	%	%	%
Ventricular Extrasystoles	312 (24.1)	2 (0.7)	6 (14.6)	2.5
Parcial AV Block	75 (5.8)	2 (3.1)	3 (27.2)	6.6
Total AV Block	60 (4.6)	14 (32.5)	11 (64.7)	41.6
Atrial Tachycardia	22 (1,7)	0	1 (11.1)	4.5
Atrial Fibrilation and Flutter	57 (4,4)	0	7 (38.8)	12.2
Ventricular Tachycardia + Ventricular Fibrillation	36 (2.7)	16 (59.2)	8 (88.8)	66.6
Asystole	60 (4.6)	35 (100)	23 (92.0)	96.6
Cardiogenic Shock	27 (2.0)	14 (93.3)	12 (100)	96.2
Acute Pulmonary Edema	17 (1.3)	9 (75.0)	5 (100)	82.3
Heart Failure	14 (1.0)	5 (35.7)	0	35.7

Table 4

Infarcting Clinical Picture

Importance of Prognostic Factors:
Sex, Age, crisis/Hospitalization and Enzymatic Peaks

Índices of Mortality

			Cases	Mortality	%
			1109	136	12,2
Sex		**Female**	191	36	18.8
		Male	918	100	10.8
Age		**<70y**	956	93	9.7
		>70y	153	43	28.1
Crisis/Hospitalization		**<6 hours**	586	53	9.0
Interval		**>6 hours**	523	83	15.8
Enzymatic	**ICP-H**	**<3xN**	708	7	0.9
Peaks	**ICP- I**	**>3xN**	401	129	32.1

Table 5

Infarcting Clinical Picture

Importance of Crisis/Hospitalization Interval (<6horas or >6h)
Related with Sex and Age on Mortality

Crisis/Hospitalization Interval: <6h				**Crisis/Hospitalization Interval: >6h**		
Cases	**Mortality**		**%**	**Casos**	**Mortalidade**	**%**
586	**53**		**9.0**	**523**	**83**	**15.8**
Sex Factor						
Female:	85	11	12.9	106	25	23.5
Male:	501	42	8.3	417	58	13.9
Age Factor						
<70 years	530	41	7.7	426	52	12.2
Female:	74	10	13.5	71	12	16.9
Male:	456	31	6.8	355	40	11.2
>70 years	56	12	21.4	97	31	31.9
Female:	11	1	9.0	35	13	37.1
Male:	45	11	24.4	62	18	29.0

Table 6

Confrontation of Groups ICP- H and ICP- I

(Predominant Mortality:

Crisis/Hospitalization Interval >6h; Female and Age >70 years)

Infarcting Clinical Picture: 1109 patients

	Cases	Mortality			Cases	Mortality	
		Nro.	%			Nro.	%
ICP-H	708	7	0.9	**ICP- I**	401	129	32.1
				Crisis/Hospitalization <6 hours: 586 pts			
<6h	380	1	0.2	**< 6 h**	206	52	25.2
Female	60	1	1.6	**Female**	25	10	40.0
<70y	52	1	1.9	**<70y**	22	9	40.0
>70y	8	0	0	**>70y**	3	1	33.3
Male:	320	0	0	**Male:**	181	42	23.2
<70y	299	0	0	**<70y**	157	31	19.7
>70y	21	0	0	**>70y**	24	11	45.8
				Crisis/Hospitalization >6 hours: 523 pts			
>6h	328	6	1.8	**>6h**	195	77	39.4
Female	72	2	2.7	**Female**	34	23	67.6
<70y	51	0	0	**<70y**	20	12	60.0
>70y	21	2	9.5	**>70y**	14	11	78.5
Male:	256	4	1.5	**Male:**	161	54	33.5
<70y	221	3	1.3	**<70y**	134	37	27.6
>70y	35	1	2.8	**>70y**	27	17	62.9

Faced with all that was appreciated, representing changes in the clinical evolution never before observed, we have established the early ambulation, pioneer (1972) and revolutionary, for the time in which was only allowed after 7-8 weeks of bedrest, taking into account solely the enzymatic peaks. Thus, in the group identified as ICP-H, the ambulation started to occur at fifth day and ICP-I in the tenth day with the hospital discharge on the following day, with the recommendation of relative rest in their own home, under the maintenance therapy with the first return to the clinic on the twentieth day.

The mortality coincident with early ambulation was 0.4% (5 cases).

About the cardiotonic effects on the ECG, we have recorded: 1) the dominant regressive tendency and often surprising aspects of early generation in activation of areas formerly mute or unexcitable - Q or QS deflections, 2) the peculiar behavior of the RS-T segment and of T wave in few days of hospitalization, which is very curious and exceptional, never registered before in any other forms of treatment, characterized by four successive stages, 3) and also constituting a particularity of the

cardiotonic effect, has been the early record and transience of the coronary T wave, escaping the rule of their lasting behavior (Table 7).

Table 7

Peculiarities of ECG in Infarcting Clinical Picture, treated with cardiotonic (Strophantin or Digitalis): 4 Stages of RS-T Segment and T Wave

I Stage – Single phase wave: RS-T segment and T wave (+)

II Stage: Fall in RS-T segment and tendency to biphasic T wave (Type +-) Negativity, sometimes with coronary aspect, of short duration

III Stage: Again, RS-T segment with horizontal depression and positive T wave

IV Stage: Return of RS-T segment to baseline and evolutive T wave to negativity, passing by biphasic T wave (Type +-)

Residual curves of infarction without permanent coronary T wave, Expresses Regressive Trend of Changes of QRS complex

In our first publication (1) on the effects of the new therapeutic routine in the infarcting clinical picture, showing up advantageous, beneficial, essential and decisive, we highlight the following results:

- Absolute tolerance to the drug
- Reduction in administration of analgesics and narcotics
- Low incidence of cardiac arrhythmias
- Low incidence of heart failure
- Low incidence of cardiogenic shock
- Low relative peaks of enzymatic reactions
- Low mortality
- Clinical Picture more calm and safe.

Discussion

The major purpose of this study is the disclosure of the myogenic theory of myocardial infarction with new concepts of pathophysiology and therapeutic, placed in confrontation with the Theory Thrombogenic through successive papers since 1972 (1-12).

We have shown that a simple therapeutic which is available to physicians and patients, escaping entirely from the current orthodox principles, and not justified within the concepts of the Thrombogenic Theory, demonstrate itself capable of producing great changes in patients with infarcting clinical picture in its clinic evolution in the Coronary Care Unit, mainly characterized by low rates of Mortality and Morbidity (Tables 3, 4, 5 and 6).

We can proclaim, emphatically, that the cardiotonic in the infarcting clinical picture is shown essential, safe, unsurpassed, successful and generator of major changes in the evolution of this clinical condition by burying archaic concepts, competently and speculatively invalidated by several clinical studies in its use in the infarcting clinical picture (44-51). Also, formally, through the experimental findings made by Puri in the acute myocardial infarction (52). This was followed by many other experimental studies (53-55) that came to break the taboo of the use of cardiotonic drugs in the acute myocardial infarction, without heart failure.

Furthermore, we reiterate our preference for strophanthin G or K, intravenously, in infarcting clinical picture, as the cardiotonic electively better and always safe in heart failure, consecrated among us in the past and in routine use in European countries but abandoned in Brazil since the 80s, as a consequence of the current lamentable lack of identification of the Brazilian cardiology with our past, of profitable European inspiration.

Its compulsory ban occurred because of the lack of identity of the Brazilian cardiology dependent of the dominating influence from U.S., that strangely, does not use the strophanthin in the Clinic, a very old complaint formulated by Bruno Kisch (1944) (56) , which was confirmed by us in a visit to U.S. (1954).

In the treatment of infarcting clinical picture, we have demonstrated that our therapeutic routine is capable of halting the evolving process to the infarction, since the pathophysiological mechanism developed by us, is initiated by Regional Myocardial Insufficiency. Consequently, being able to prevent the myocardial necrosis by the correction, in time, of the predominant regional myocardial dysfunction. Moreover, it can promote the rescue of the viable myocardial fibers or at least attenuate the necrotic process and reduce the infarct size.

The effects of the association of the cardiotonic + coronary dilator on the infarcting clinical picture, seem to us to be overwhelmingly demonstrated by dividing the halted cases (ICP-H), representing 63.8% of the cases, with enzymatic peaks inferior to three times the normal and very low mortality (0.9%), and the infarcted cases (ICP-I) representing 36.2% of the cases presenting a mortality of 32.1%, in which prevails the prognostic importance of the following factors: crisis / hospitalization interval > 6 hours; Age> 70anos and Female sex (Table 6).

It is necessary to point out, in this type of treatment, the low levels of clinical complications and mortality during hospitalization (Table 3) and, especially, the prevalence of the Age factor (> 70 years) in the prognosis (9).

With the reduction in the incidence of arrhythmias after the use of the cardiotonic, there was a projection in the cases of partial (5.8%) and total (4.6%) AV block. But, in fact, what happened was just a relative and apparent predominance of these blocks, thanks to the great reduction of other arrhythmic conditions, since its incidences do not outweigh the literature records.

In partial and total AV block, the phenomenon is seen as a direct result of the compromised coronary process, without direct involvement of the affected myocardium by the infarction. This interpretation is based on the absolute predominance of cases with electrocardiographic pattern in infarction of the inferior wall and its variations (85.2% in partial AV block and 85.4% in total AV block), dependent most times on the pathology of the right coronary artery, responsible for the irrigation of the specific muscle system and especially of the AV node.

The AV blocks are not exacerbated by the continued use of the cardiotonic and usually occurs the disappearance of the total AV block, with or without artificial pacemaker, in almost all cases, between the seventh and ninth days of evolution, with the record of only 2 cases of definitive implantation of artificial pacemaker among survivors.

Also, it is worth to mention the low incidence of Tachycardia + Ventricular fibrillation (2.7%), asystole (4.6%), and particularly, as very significant, the recorded in cardiogenic shock (2%),

referred universally with the incidence between 10 -15%. Obviously, the indices of acute pulmonary edema (1.3%) and of heart failure (1%) corroborate with the exceptional myocardial effects that characterize the essential and beneficial action of strophanthin (IV), coincident with the successes of Ernst Edens (1928-1944) (57) in Germany, who expressed himself about his results:

"After the recognition of strophanthin as the best and safest medicine, we no longer have the right to use it in a patient, only for scientific reasons and tests for unknown purposes, giving preference to other drugs and thus losing precious time for the cure "..... and expressing his evidence by saying:" there would come a time when the omission of the use of strophanthin will be seen as professional misconduct."

Rolf Dohrmann (1980) (11), also in Germany, using the strophanthin (IV) in acute myocardial infarction, obtained the same results achieved by us.

Conclusion

The cardiotonic + coronary dilator interferes directly, effectively and beneficially in the pathophysiological mechanism advocated by the Myogenic Theory, correcting the Regional Myocardial Insufficiency, halting the evolving process (ICP) for the myocardial infarction at admission, with the rescue of viable myocardial fibers, which may avoid the myocardial infarction, minimizing the area of myocardial necrosis and reducing the infarct size.

In mortality, the prevalence of prognostic factors (Sex, Age > 70 years, crisis / hospitalization interval > 6h) are evident in ICP-infarcted and insignificant in ICP-halted, seeming to indicate the importance of myocardial infarct size, surely characterized by the enzymatic peaks.

References:

1) *Mesquita QHde, Reis JP,Kerbrie SV, Mari SM, Baptista CAS, Monteiro J, e Ribeiro DDL: Efeitos da Estrofantina-K de uso endovenoso, no tratamento do quadro clínico enfartante e do enfarte agudo do miocárdio, RBCTA, 1973;2:647*
2) *Mesquita QHde, Kerbrie SV, Mari SM, Baptista CAS, Monteiro J e Ribeiro DDL: Teoria Miogênica do enfarte do miocárdio. Novos conceitos de Fisiopatologia e Terapêutica, Trabalho apresentado ao 31° Congresso Brasileiro de Cardiologia, Julho, 1975*
3) *Mesquita QHde, Anticoagulante e enfarte miocárdico, Publicações Médicas, 1962;211:3*
4) *Mesquita QHde, Baptista CAS Kerbrie SV, Mari SM, Monteiro J e Maciel MC: Proteção do miocárdio no quadro clínico enfartante pela estrofantina endovenosa, Arq Bras Cardiol, 1976;29 (supl. 1):439*
5) *Mesquita QHde, Baptista CAS, Kerbrie SV, Mari SM, Monteiro J e Maciel MC: Valor prognóstico dos subsídios enzimáticos e eletrocardiográficos no enfarte agudo do miocárdio tratado por Estrofantina, Arq Bras Cardiol, 1977;30 (supl. 2):393*
6) *Mesquita QHde: Teoria Miogênica do enfarte do miocárdio. Novos conceitos de fisiopatologia e terapêutica, Edição do autor, 1979 (Myogenic Theory of Myocardial Infarction – Book, Download free of Charge - Summary in English at http://www.infarctcombat.org/MyogenicTheory.html)*
7) *Mesquita QHde: Cardiotônico e enfarte agudo do miocárdio no homem, RBCTA,1981;10:645*
8) *Mesquita QHde: Aspectos angiográficos coronários e ventriculográficos do primeiro enfarte do miocárdio em coronariopatia crônica silenciosa, Rev Bras Med, 1982;39:427*
9) *Mesquita QHde: Importância da Idade como fator prognóstico do enfarte agudo do miocárdio, Rev Bras Med (Cardiologia),1983;2:335*
10) *Mesquita QHde: Implicações fisiopatológicas e terapêuticas do enfarte agudo do miocárdio e coronárias angiograficamente normais ou com lesões estenóticas pérvias, Rev Bras Med (Cardiologia), 1985;4:187*
11) *R.E.Dohrmann; H.D.Janisch & M.Kessel: Klinisch-poliklinische Studie über die Wirksamkeit von g-Strophanthin bei Angina pectoris und Myokardinfarkt,; Cardiol Bull (Cardiologisches Bulletin) 14/15: 183-187, 1977*
12) *Mesquita QHde, Baptista CAS: Porque Teoria Miogênica e não Teoria Trombogênica; Arq Bras Cardiol: Vol 62 (nº 4), 1994*
13) *Mesquita QHde: Nova e simplificada classificação eletrocardiográfica do enfarte agudo do miocárdio, Rev Bras Med (Cardiologia), 1985;4:34*

14) *Mesquita QHde e Baptista CAS: Eletrocardiograma do infarto ventricular direito – Evolução histórica e crítica, Ars Cvrandi, 1995;28:12-44*
15) *Coll S, Castaner A, Sanz G, Roig E, Magrina J, Navarro-Lopez E e Betrin A: Prevalence and prognosis after a first nontransmural myocardial infarction, Am J Cardiol, 1983;51:1584*
16) *Gibson RS, Beller GA, Gheorghiade M, Nygaard TW, Watson DD, Huey BL, Sayre SL, e Kaiser DL: The prevalence and clinical significance of residual myocardial ischemic 2-weeks after uncomplicated non-Q-wave infarction: a prospective natural history, Circulation, 1986;73:1186*
17) *DeWood MA, Stifter WF, Simpson CS, Spores J, Engste G, Judge TP, e Hinnem ML: Coronary arteriographic findings soon after non-Q-wave myocardial infarction, N Engl J Med, 1986;315:417*
18) *Ogawa H, Hiramori K, Haze K, Saito M, Sumiyoshi T, Fukami K, Goto Y, e Ikeda M: Comparison of clinical features of non-Q-wave and Q-wave myocardial infarction, Am Heart J, 1986;111:513*
19) *Ambrose JA, Craig E, Monsen H, Borrico S, Gorlin R, e Fuster V: Angiographic demonstration of a common link between unstable angina pectoris and non-Q-wave acute myocardial infarction, Am J Cardiol, 1988;61:245*
20) *Andre-Fouet X, Pillot M, Leizorowicz A, Finet G, Gayet C e Milon H: Non-Q-wave, or "nontransmural" myocardial infarction: a specific entity, Am Heart J, 1989;117:892*
21) *Saphir O, Ohringer L e Wong R: Changes in the intramural coronary branches in coronary arteriosclerosis, Arch Path (Chicago), 1956;62:159*
22) *Spain DM e Bradess VA: The relationship of coronary thrombosis to coronary atherosclerosis and ischemic heart disease (a necropsy study covering a period of 25 years), Am J Med Sci, 1960;240:701*
23) *Spain DM e Bradess VA: Frequency of coronary thrombosis related to duration of survival from onset of acute fatal episodes of myocardial ischemia, Circulation, 1960;22:816*
24) *Erhardt LR, Lundman T, e Mellstedt H, Incorporation of I 125 labelled fibrinogen into coronary arterial thrombi in acute myocardial infarction in man, Lancet, 1973;1:387*
25) *Erhardt LR, Unge G, e Boman G: Formation of coronary arterial thrombi in relation to onset of necrosis in acute myocardial infarction in man, a clinical and autoradiographic study, Am Heart J, 1976;91:592*
26) *Roberts WC, Coronary arteries in fatal acute myocardial infarction, Circulation, 1972;45:215*
27) *Eliot RS, Baroldi G e Leone A: Necropsy study in myocardial infarction with minimal or no coronary luminal reduction due to atherosclerosis, Circulation, 1974;49:1127*
28) *Bulkley BH, Klacsmann PG e Hutchins GM: Angina pectoris, myocardial infarction and sudden cardiac death of 9 patients with progressive systemic sclerosis, Am Heart J, 1978;95:563*
29) *Baroldi G: Acute coronary occlusion as a cause of myocardial infarct and sudden coronary heart death, Am J Cardiol, 1965; 16:899*
30) *Baroldi G: Editorial. Coronary heart disease: significance of the morphologic lesions, Am Heart J, 1973;85:1*
31) *Baroldi G: Coronary thrombosis: facts and beliefs, Am Heart J, 1976; 91:683*
32) *Baroldi G: Different types of myocardial necrosis in coronary heart disease. A pathophysiologic review of their functional significance, Am Heart J, 1975;89:742*
33) *Morgan AD: The pathogenesis of coronary occlusion, Springfield, Illinois, Charles C. Thomas, 1956*
34) *Edwards JF: What is myocardial infarction, Circulation, 1969,40 (suppl IV):5*
35) *Hackel DB: Some problems concerning coronary artery occlusion and acute myocardial infarction, Circulation, 1969;40(suppl IV):3*
36) *Donomoe I, Matsumoto Y, Kojubu T, Koide R, Kobayashi R, Iregami H, Ueda E, Fujisawa T e Fujimoto S: Pathological studies of coronary atherosclerosis; especially of sclerosis of intramuscular coronary arteries, Jap Heart J, 1962;3:423*
37) *Ehrlich JC e Shinohara Y: Low incidence of coronary thrombosis in myocardial infarction. A restudy by serial block technique, Arch Path (Chicago), 1964; 78:432*
38) *Brest AN, Myocardial infarction without obstructive coronary artery disease, Am Heart J, 1974;88:219*
39) *Roberts WC: Coronary thrombosis and fatal myocardial ischemia, Circulation, 1974:49:1*
40) *Murakami et al: Intracoronary aspiration thrombectomy for acute myocardial infarction, Am J Cardiol 1998 Oct 1;82(7):839-44*
41) *O'Neill, WW:Editorial. Coronary thrombosis during acute myocardial infarction: Roberts was right!, Am J Cardiol 1998 Oct 1; 82(7): 896-7*
42) *Chandler AB e col.: Coronary thrombosis in myocardial infarction. Report of a workshop on the role of coronary thrombosis in the pathogenesis of acute myocardial infarction, Am Heart J, 1974;34:823*
43) *Hellstrom HR, Myocardial infarct as a cause of coronary thrombosis, Circulation, 1970;42 (supp III):165*
44) *Askey JM: Digitalis in acute myocardial infarction, JAMA, 1951; 146:1108*
45) *Boyer NH: Digitalis in acute myocardial infarction, N Engl J Med, 1955;252:536*

46) *Malmcrona R, Schroder R e Werko L: Haemodynamic effects of digitalis in acute myocardial infarction, Acta Med Scand, 1966;180:55*
47) *Constant J: Digitalis in Myocardial infarction, NY State J Med, 1970;70:650*
48) *Pizzarello R, Reduto L, Geller K, Gullotta S e Morrison J: Protection of the ischemic myocardium in man by digitalis, Circulation, 1975;51-52 (suppl II):895*
49) *Morrison J, Pizzarello R, Reduto L e Gullotta S: Effect of digitalis on predicted myocardial infarct size, Circulation, 1976;53-54 (suppl II):102*
50) *Reicansky I, Conradson TB, Holmberg S, Ryden L, Waldenstrom A, Wennerblom B: The effect of intravenous digoxin on the occurrence of ventricular tachyarrythmias in acute myocardial infarction in man, Am Heart J, 1976;91:705*
51) *Loeb HS, Sinno MZ, Rahimtoola SH, e Gunnar RM: Effects of Ouabain on early ventricular relaxation in patients with acute myocardial infarction, Chest, 1976;70:259*
52) *Puri RS: Modification of experimental myocardial infarct size by cardiac drugs, Am J Cardiol, 1974;33:521*
53) *Kerber RE, Abboud FM, Marcus ML e Eckberg DL: Effect of inotropic agents on the localized dyskinesis of acutely ischemic myocardium. An experimental ultrasound study. Circulation, 1974;49:1038*
54) *Banka VS, Bodenheimer MM, Helfant RH e Chadda KD: Digitalis in experimental acute myocardial infarction. Differential effects on contractile performance of ischemic border and nonischemic ventricular zones in the dog, Am J Cardiol, 1975;35:801*
55) *Vatner SF e Baig H: Comparison of the effects of Ouabain and isoproterenol on ischemic myocardium of conscious dogs, Circulation, 1978;58:654*
56) *Kisch B: Strophanthin, Brooklyn Medical Press, New York City, NY, 1944*
57) *Ernst Edens, Munchener Medizinischen Wochenschrift; 37, 1934; Peter Schmidsberger, So Bekämpft ein Brasilianer Den Herzinfarkt. October 4, 1980. Bunte, Offenburg, Germany*