The Impact Of Severity Of Ischaemia In Acute Coronary Syndrome On The Extent Of Coronary Artery Disease At Angiography The Role Of Past Ischaemia

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Summary:

Background: *Clinical classification of patients with acute coronary syndrome is essential step in identifying severe cases before referring them, fairly quickly, for the ultimate investigation of coronary angiography .Hence it is important to find out the extent at which the severity of the disease, based on clinical classification, agrees with its severity at angiography and to see whether traditional Risk factors or pas ischaemia played a role.*

Patients and Methods : *The angiographer data of 178 consecutive pts with Acute Coronary Syndrome (ACS) were retrospectively analyzed. The pts consisted of 114 with Unstable Angina (UA) and 64 pts with Non-ST-Segment Elevation Myocardial Infarction (NSTEMI). Patients were classified depending upon the predominating clinical assessment during hospitalization into four groups of progressively worsening ischaemia. They were; group 1; New onset Angina; 27 pts, group 2; Deteriorating Chronic Angina, 33 pts, group 3; Rest Angina 54 pts, and, group 4; Non-ST-Elevation Myocardial Infarction (NSTEMI), 64 pts.*

Results : *Coronary Angiography revealed that the frequency of multi-vessel coronary Disease (MVD) in group 1, 2, 3, and 4 were 48%, 73%, 72%, and 56% respectively which meant that worsening of ischaemia was not accompanied by commiserate increase of the frequency of MVD in Rest angina and NSTEMI. To explain that we calculated the average number of Five traditional Risk Factors; Hyperlipidaemia (HL), Diabetes Mellitus (DM), Hypertension (HTN), Smoking (SM), and Positive Received March 2006 Family History (PFH) in the four groups ofACS (R.F. score) and they were 1.72, 1.87, 2.13, 2.51 in Accepted May 2006 groups 1,2,3, and 4 respectively. Then we studied the relation of having one, two, three, and four orfive Risk Factors and the frequencies of Multi-vessel disease and they were; 43%, 67%, 76%, and 84% respectively which meant that the frequency of MVD ought to increase from group 1 to group 4 supporting the clinical classification. This prompted us to look into the individual Risk factors. The clinical data showed that the incidence of HL had risen significantly in Ch. D. angina and Rest Angina (P: 0.03) and that the incidence of SM had risen significantly in NSTEMI (P.• 0.001). Since the angiographic data had demonstrated a significant association of HL with MVD and SM with SVD we may understand why the rate of MVD was not higher in NSTEMI than UA. To explain why the frequency of MVD in Rest Angina (g. 1) was not higher than Ch. D. Angina (g. 2) despite having worse ischaemia and higher R.F. Score we scrutinized the data and noticed that the main difference between group 1 and group 2 that chronic stable angina had preceded the onset of UA in Group 2 while it did not do in group 1. On the other hand Rest Angina and NSTEMI pis were a mixture of those with and without prior ischaemia. To follow this point further we divided both groups into two subgroups: one with history of prior ischaemia and one without it. The frequency of MVD in Rest Angina and NSTEMI with prior ischaemia were 83%% and 81 %% compared to 54% and 39% respectively in pts without it.*

Conclusion *this study has shown that clinical classification in Acute Coronary Syndrome may predict severity of the underlying CAD to some extent however considering the no. Of risk factors and which Risk factor and whether there was antecedent ischaemia would improve the prediction a great deal.*

Key Words: *patient = Pt, Traditional Risk Factor =TRF, Hyperlipidaemia = HL, Diabetes Mellitus = D.M., Hypertension = HTN, Smoking = SM, Positive Family History for Ischaemic Heart Disease = P.F.H, Coronary Artery Disease =CAD.*

Introdution:

Acute Coronary Syndrome is a serious manifestation of atherosclerosis (1). It is comprised of non-homogenous groups of patients with variable outcome (2). Some pts has mild underlying disease involving a branch of main Artery others may has severe disease involving all three major coronary with poor prognosis unless revascularization was contemplated (3). Patients are usually classified depending on their predominating clinical feature, which intended to put them in groups of increasing ischaemia. This aimed at identifying a subset of patients with severe disease who would be referred, fairly early, for the ultimate investigation of coronary angiography which demonstrate the underlying disease and its severity. In this study we are trying to see to what extent clinical classification predicts the severity of the underlying disease and study the role of risk factor in that matter and the impact of having antecedent ischaemia on the severity of the underlying disease (4,5,6)

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Patients and Methods:

The data of 188 pts with Acute Coronary

syndrome were retrospectively analyzed. They were admitted to Dalian Hospital in Reyiad between 1998 and 2001 and the Medical City in Baghdad between 2002 and 2003.

Secure diagnosis is based on typical presentation and course. Typical presentation with characteristic chest discomfort/ pain that is poorly localized in the anterior chest or left arm. The symptom has at least one of the following features. It occurred on minimal exertion or at rest and usually lasts for up to 2030 minutes. The pain response to sublingual Nitroglycerine is not usually prompt (It usually needs larger dose). The pains had crescendo pattern being severe, prolonged, and more frequent than previously. Atypical symptoms, such parascapular pain, or pain-equivalent symptoms required confirmation of ischaemic origin through objective evidence, by either transient ECG changes or transient hypokinesia on the echocardiogram.

In pts with NSTEMI the pain had to be much longer. The diagnosis of NSEMI required the confirmation of cardiac muscle necrosis by Cardiac Enzymes.

Ten pts who had no or non-significant coronary artery lesion were excluded. The remaining 178 pts data, which included 17 pts with no risk factors, were retrospectively analyzed. They consisted of 114 pts with UA and 64 pts with NSTEMI.

The UA pts were classified into three groups of progressively worsening ischaemia based on their predominating clinical findings and noninvasive investigations during hospitalization. The three groups were;

A. New-onset severe Angina; (group 1) 27 pts. B. Deteriorating Ch. Angina; (group 2) 33 pts. C Rest Angina (group 3) 54 pts.

The classification was inspired by Eugene Braunwald 1989 classification but it was not possible to comply with it strictly. One important cause was the fact the no. pts without chest pain or its equivalent during the last 48 hrs was too small.

D. The 64 pts with NSTEMI were regarded as group 4

All NSTEMI pts and most UA pts were admitted to the Coronary care unit. Some pts with UA were admitted to the intermediate care unit when the CCU is full. All pts were given the standard treatment with nitrate and Heparin infusion, Aspirin, Beta-blockers, and Statins. AC-Inhibitors were given to pts with LV dysfunction. Abciximab was given to some pts with NSTEMI and UA during catheterization with possible intervention in the presence of a thrombus. Coronary angiography was done during hospitalization or soon after discharge. Coronary lesion was regarded significant if the narrowing cut down the lumen by >70. > 50% Left Main stem disease was regarded equivalent to two vessels disease

Results

A. Severity of CAD in the various groups of ACS

The data showed that the incidence of Multi-vessel Coronary Artery disease ; Significant lesions involving two or three main coronary arteries had increased from 48% in patients with New-Onset Angina (group 1) to 73% in pts with chronic deteriorating Angina (group 2), stabilized at 72% in Rest Angina (group 3), then declined to 56% in pts with NSTEMI (group 4) suggesting that the angiographic findings had agreed with the clinical classification in reflecting the severity of underling CAD, as judged by the frequency of multi-vessel disease, in pts with Chronic deteriorating Angina only . Unexpectedly there was no further rise of the incidence of MVD in Rest Angina and in NSTEMI See table -1

Table -1- shows the incidences of both SVD and MVD in the various ACS groups.

Severity of CAD	Group I UA 25 pts	Group 2 UA 30pts	Group 3 UA 47 pts.	NSTEMI 59 pts
SVD	13 52%	8 27%	13 27%	26 44%
MVD	12 48%	22 73%	34 72%	33 56%
Note: - seventeen ots with no Risk were not included in table 1. 2. 4. 5. and 6				

B. Risk Factors score in ACS

Searching for an explanation for this discordance between clinical and angiographic findings we looked into the number of the Risk Factors in the four groups of pts with acute coronary syndrome. Table -2-showed that the no. of the Risk Factors for each patient (Risk Factor score) had progressively increased from 1.72 in group 1 to 1.87 in group 2, to 2.13 in group 3, and to 2.51 in group 4 suggesting that clinical severity was associated with higher

Risk Factor score. See Table -2

Table -2-this showed the relationship of average no. of Risk Factors per pt in the various ACS rou s

group /MRF	Group I (NOA) 25 pts.	Group 2(DCA) 30 pts	Group 3 (RA) 47 pts	NSTEMI 59pts.
NoofMRF	43	56	102	148
MRF per pt. (MRF score)	1.72	1.87	2.13	2.51

C. Severity of CAD in increasing no. of Risk Factors

To study the relationship between the number of the Risk Factors the severity of CAD we looked at the frequency of one, two, three vessel disease and Multi-vessel in the pts with one, two, three, and four or five Risk Factors and found that more than half of the 54 pts with one Risk Factor (57%) had significant lesion/s in one of three main coronary arteries (Single Vessel Disease; SVD) It also showed that the incidence of SVD had progressively diminished to from 82%in pts with no Risk Factor to 57%, 31%, 24%, and 17% in those with two, three, and four-five Risk Factors respectively. Conversely the incidence of three vessels Disease (TVD) had increased progressively from 6% in pts with no Risk Factor to 19%, 33%, 51%, and 66% in pts with one, two, three, and 4-5 Risk Factors. The same trend was apparent in the incidence of MVD where it had risen froml8% in pts with no Risk factor to 83% in those with 4-5.. See table 3

Table -3- The relationship of the no. of Risk Factors and the severity of the coronary disease

RFND		Single VD		Two VD		Three VD		Multi-VD		P.V.
NHRF	17	14	82%	2	12%	1	6%	3	18%	
OneRF	-54	31	57%	13	24%	10	19%	23	43%	
TwoRF	52	16	31%	19	37%	17	33%	36	69%	
Three RF	37	9	24%	9	24%	19	51%	27	76%	
4-5 RF	18	3	17%	3	17%	12	66%	16	83%	

Comparing the first and the last rows in table -3- reflect the severity of CAD in the two extremes. It shows that 82% of pts with no MRF had SVD Compared to only 17% of pts with 4-5 MRF, indicating that although Risk factors may determine the severity of the disease CAD can occur without them and if so iit would likely to be much milder.

D. Predisposition to the various groups of UA by the risk factors

Though pts with Rest Angina and NSTEMI (group 3 and group 4) has more ischaemia and higher Risk factor score there was no commiserate increase in the rate of Multi-Vessel Disease. This prompted us to identify the risk factors in each group and study their role in the predisposition to the various groups. Table -4- shows that D.M, HTN, SM, and PFH predisposed nearly equally to three groups of UA while the incidence of HL had increased from 40% in pts with group 1 with New-Onset Angina to 67% in the pts with Deteriorating Chronic Angina and to 70% in pts with Rest Angina RA indicating that HL significantly predisposed to severe UA.

Table -4- showed the predisposition to the various groups of UA by the Risk Factors.

Group IRF		Group I (NOA) 25 pts.		Group 2(DCA) 30 pts		P. Value	Group 47 Rest Angina	
HL	93	10	40%	20	67%	0.05	33	70%
D.M	75	9	36%	12	43%	N.S	23	49%
HTN	77	11	44%	13	43%	=	21	45%
SM	67	8	32%	8	27%	=	14	30%
PFH	38	5	20%	3	10%	=	11	23%

E. Predisposition to UA and NSTEMI

Table -5- shows that the contribution by all Risk factors to the predisposition to Un and NSTEMI was not statistically different apart from SM which had predisposed more significantly to NSTEMI than to UA; 58% compared to 29% respectively. PFH had the same trend.

Table -5 - Comparison of the predisposition by the risk factors to UA and NSTEMI.

Main Risk Factors	Unstable Angina 102 pts.	NSTEMI 59 pts.	P Value
Hyperlipidaemia	63 62%	30 51%	N.S
D.M	44 43%	32 54%	N.S
HTN	45 44%	32 54%	N.S
Smoking	30 29%	3458%	< 0.001
Positive F.H	19 19%	20 34%	<0.03

F. Severity of CAD in isolated Risk Factors

To find the relationship of each Risk Factor and the severity of coronary artery disease we studied the frequency of multi-vessel disease in the 54 pts with single Risk factor only. We found that the incidence of MVD in association with SM, HI, D.M, HTN, and PFH, were; 20%, 62%, 70%, 40%,and 17%, which shows that Smoking and PFH was associated more with SVD than MVD and that Hyperlipidaemia and Diabetes Mellitus were associated more with MVD than SVD. (See table -6-).

Table -6- Relationship of the severity of Coronary Artery disease and each Risk Factor of the pts with one Risk Factor.

Risk Factors	Severity of CAD		P. Value
	Single - vessel Disease	Multi-vessel Disease	
Smoking 15 pts	12 80%	3 20%	} P.V. = 0.03
Hyperlipidaemia 13 pts	5 38%	8 62%	
Diabetes Mellitus 10 pts	3 30%	7 70%	
Hypertension 10pts	6 60%	4 40%	
Positie F.H.	5 83%	1 17%	

The clinical data had shown that Hyperlipidaemia was the most frequent Fisk factor in group 2 and 3 UA while Smoking was the most frequent Risk Factor in the group 4 of NSEMI. Since the angiographic data showed that HL was predominately associated with multi-vessel disease while Smoking was associated with Single Vessel Disease we may explain the reason behind the discordance between the clinical and the angiographic findings in pts with Non-ST-Elevation Myocardial Infarction

The Role of Past Ischaemia

Since rest Angine compared with chronic Deteriorating angine , had more ischaemia on clinical classification and had higher R.F. score it would have been expected that the incidence of MVD would also be higher but it was not. Looking for an explanation we studied the role of having any ischaemic event prior to presentation. It appears that the main difference between group 2 and group 1 was that group 2 pts had the disease much longer starting with chronic stable angina that had later degenerated into Unstable Angina while in group 1 the disease began as Denovo UA. The pts in groups 3 and 4 were a mixture of both types. Consequently we dividedtht pts in

group 3 and 4 into two subgroups; one a "denovo" subgroup and the other "with prior ischaemia" subgroup . The result was striking. Table 7 (see below) showed that the incidence of MVD was 54% and 45% in the "Denovo" subgroups, compared to 83% and 81% in the " with prior ischaemia" subgroups . These findings suggest that a clinico-angiographic classification of ACS if it took into consideration whether the patient is known to have IHD from before or not when a pt. is known tohave IHD develops UA, or sustains NSTEMI he or she is very likely to have much more severe underlying coronary disease in the way of two or three vessels disease than a pt. Who has not. who has not. a pt. is known to have IHD develops UA, or

Table 7 shows comparison between the subgroups of patients with and without prior ischaemic events.

Main Group	Subgroup 3-a	Subgroup 3-b	P. Value
Rest UA 54 SVD16 MVD 38	Rest UA Denovo 24 SVD 11 46% MVD 13 54%	Rest UA with prior isch. 30 SVD 5 17% MVD 25 83%	0.02
NSTEMI 64 SVD 26 MVD 38	NSTEMI Denovo 38 SVD 21 55% MVD 17 45%	NSTEMI with prior isch. 26 SVD 5 19% MVD 21 81%	<0.01

This highlights the importance of Past Cardiac history in predicting the severity of the underlying Coronary Artery Disease. Consequently it may be feasible to consider classifying ACS into three Groups; each consists of two subgroups. They are: -

Group "la - Denovo Exert ional UA. Group lb- Exertional UA with Prior Ischaemia Group 2a - Denovo Rest UA. Group 2b - Rest UA with prior Ischaemia

Group 3a - Denovo NSTEMI. Group 3b - NSTEMI with prior Ischaemia

Discussion

Clinical classification of patients with acute coronary syndrome is essential step in identifying severe cases before referring them, fairly quickly, for the ultimate investigation of coronary angiography (1,2.3). To find out the extent at which the severity of the disease, based on clinical classification, agrees with its severity at angiography this study had shown that worsening of the ischaemia was accompanied by deterioration of the underlying coronary artery disease in" Moderately severe Unstable Angina ie Chronic Deteriorating Angina" but not in "Very severe:"one ie Rest Angina and also in NSEMI.

Looking for an explanation we addressed the role of the Risk Factors and found that the increasing the number of risk factors was associated with increase of the incidence of Multi-vessel disease. This observation was reported by Mesquita et al who found that high number of Risk Factor were more frequently associated with Multi-vessel coronary artery disease than single vessel disease (9) The Canadian atherosclerosis intervention trial (CCAIT) has characterized women with Acute coronary syndrome as having a high prevalence of Risk Factors with a large proportion of Multi-vessel Coronary Artery disease and high rate of revascularization (10). Our study also found a direct relation of Risk Factor Score ; n average umber of risk factorsin each patient and the severity of clinical ischaemia where patients with Non-ST-Elevation Myocardial Infarction had the highest Risk Factor Score. These patients would be anticipated to have the highest level of Multivessel disease but they were not , as we mentioned above .Trying to solve this discrepancy we identified the risk factors in each of the four groups and looked into the relation of each factor to the severity of the underlying disease when those factor occurred own their own we found that Hyperlipidaemia, which was significantly predominant in UA, was frequently associated with MVD while Smoking, which was significantly predominant in NSTEMI was frequently associated with SVD. The association of Hyperlipidaemia and multi-vessel disease were reported earlier by Wang XL from Australia (11). On the other hand he tendency of smokers to have less extensive was reported by Chen etal from St. Georges Hospital of London, however the association, in their study, was more significant in pts younger than 45 years (12). In our study although most patients were

younger than 50 years the occurrence of single vessel disease had no age limit.

This may explain why pts with NSEMI did not have worse underlying coronary disease than UA however it did not explain why patients with Rest angina did not have worse coronary disease than Ch. deteriorating Angina. To find a reason we addressed the issue pas ischaemia we as we noticed that patients with Rest angina and angina tended to have more extensive underlying disease (13). This finding highlights the potential importance of prior ischaemia in clinical classification of these patients.

Conclusion this study has shown that clinical classification in Acute Coronary Syndrome may predict severity of the underlying CAD to some extent however considering the number of risk factors, which risk factors, and whether there was antecedent ischaemia would improve the prediction a great deal

References

L American Heart Association: 2004 Heart and Stroke Statistical update;. (www americanheart.orp)

2 Braunwald E. Unstable Angina: a classification. Circulation 1989; 80:410-414.

3. Braunwald E,Unstable angina:A classification, Circulation810-410,1989 etal:ACCAHAguideline updatefor the management of instable angina and non-st- segment elevation myocardial infarction. A report of the American College of Cardiology/ American Heart Association Task Forceon practice guidelines (Committee on the Management of unstableangina)wwwacc.org2002:acssessed3/15/2002

4 Antman EM etal The TIMI risk score for unstable angina/non ST-elevation MI A method for prognostication and therapeutic decision making.JAMA 284;835. 2000.

5 Yeghizaririans Y, Brunstien JB, ASKERI A, Stone PH. Unstable Angina Pectoris, NEJM 2000;37(2): 101-15.

6 Assmann G, Schulte J etal The Prospective Cardiovascular Minister relationship to coronary heart disease Am Heart J 1988;116:1713-24

Z MR FIT research group Multiple Risk Factor Intervention Trial. Risk factor changes and mortality results JAMA 1982;248:1465-77

8 The sixth report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med 1997; 157; 2413. 9.Mesquita A, Trabulo M, Ventosa A. Gill V, Scabra-Gomes R, Unstable Angina Coronary disease in women-risk factors, diagnostic and therapeutic approaches Rev Port Cardiol 1996 Apr, 15($):303-9.272.

1Q aters D, Lespeerance J, Gladstone P, Boccuzzi SJ, CooK T etal: Effects of Cigarette smoking on the angiographic evolution of coronary atherosclerosis, a Canadian Coronary Atherosclerosis Intervention Trial (CCAIT) Sub study. CCA TT Sub study Group: Circulation. 1996Aug 15,94(4):614-21.

11. Wang XL, Tarn C, McCredie RM, WilckenDE :Detrminenant of the severity of coronary artery disease in Australian men and women: Circulation. 1994May;89(5): 197481.

12 Chen 1, Chester M,Kaski JC Clinical and Angiographic features associated with premature coronary artery diseaseChestl995 Aug. 108(2):364-9 13De Zwaan C, Bar FW, Georgels AG, Wellens HJ. Unstable Angina; are we able to recognize high risk patients Chest. 1997 jul;112(l);244-50.