Coronary Artery Lesions In Patients With Acute Coronary Syndrome. The Role Of The Traditional Risk Factors

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Summery:

Background and aim: *Manifestations of Acute Coronary Syndrome (ACS) are mainly related to the underlying Coronary Artery lesions hence it is of crucial importance to study the nature of those lesions and assess the factors that might affect them, especially so the role of traditional Risk Factors in that regard.*

Material and Methods *; The clinical and angiographic data of 161 consecutive patients with Coronary Syndrome were retrospectively analyzed. They consisted of 102 pts with Unstable Angina and 59 with Non-ST-Segment Elevation Myocardial Infarction. Coronary Artery lesion was regarded significant if it caused >70% luminal narrowing. Left Main stem lesion {> 50%} was regarded equivalent to two main coronary arteries lesions.*

Results *: The angiographic data of the 54 pts with only one Risk factor had shown that there were 132 significant coronary artery lesions involving the main coronary arteries. Forty lesions were reported in the 13 pts with Hyperlipidaemia (HL; 3.1), 34 lesions in the 10 with diabetes Mellitus (D.M; 3.4), 29 in the 10 pts with Hypertension (HTN; 2.9), 21 in the 15 pts with Smoking (SM 1.4), and 8 lesions in the 6 pts with Positive Family History for I.H.D (PFH; 1.3). In the same group the lesions took the form of Multiple significant stenosis involving at least two main coronary arteries were reported in 70% and 62% of the pts with D.M and HL respectively compared to a fifth of the smokers and a sixth of those with PFH ; 20% and 17% respectively in whom the lesion/s were usually discrete and confined to a single artery. Moreover the lesions were diffuse in nature in the Hyperlipidaemic and the Diabetic pts only. Lesions had led to total or subtotal occlusion of at least one main artery were reported in the Hyperlipidaemics and the Diabetics, as well, in the smokers. Smokers were the only group in whom intra-coronary thrombi and coronary ectasia were detected. Three fifths of pts with Hypertension had discrete lesions and two fifths of them had multiple ones but they had no diffuse disease .*

Note : Please remember all the above findings were reported in pts with Single Risk Factor.

The angiograms of the 52 pts with two Risk Factors showed that the presence of a second Risk Factor was associated with worsening of the coronary lesions no matter which Risk factor. However despite the considerable rise in the incidence of the multiple lesions in the Smokers and those with PFH, from their levels in pts with single Risk Factor; 61% and 45% respectively. It remained much less than their levels in pts with HL and D.M.; 79% and 80% respectively. In addition to that combination of Smoking or PFH with another Factor was associated the appearance of Diffuse lesions which were not reported when those factors occurred singularly. Coronary calcification, which was not reported in the presence of Single Risk Factors, had appeared predominately in half pts with Combined Smoking and Hyperlipidaemia.

The coronary lesions deteriorated further in the 37 pts with three Risk Factors with the exception of pts with Smoking supporting the observation that smoking tended to be associated with less severe disease. ***Conclusion;*** *— hyperlipidaemia and Diabetes Mellitus, compared to Smoking, and FH was associated more with multiple lesions and diffuse disease while Smoking seemed to be associated more with discrete lesions, as well as coronary thrombosis. Increasing the no of the Risk Factors was associated with worsening of the coronary lesions though such deterioration was less pronounced in the presence of Smoking. Key Wordsr-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.*

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Introduction:

Acute Coronary syndrome is a serious manifestation of atherosclerosis as it is associated with considerable morbidity and mortality. It is responsible for 1.4 millions admissions to hospital in the United States every year (!). ACS is caused by atherosclerosis of the coronary arteries in almost all the cases. Ever since the publication, of the report of the population based Framingham Heart Study, in the mid 1950s, work into the role of Risk Factors in the etiology of atherosclerosis and the impact of that on risk stratification has continued. That study was the first to provide support to the correlation between Hypercholesterolemia, Hypertension, and other Risk Factors and Cardiovascular disease. Subsequent work over ensuing decades and particularly during the last ten years lent great evidences supporting a direct cause and effect relation.

In this study we tried to see if there was a relation between the major traditional Risk

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Factors (Hyperlipidaemia, Hypertension, Diabetes Mellitus, Smoking, and Family History of IHD) and the nature and extent of the underlying coronary lesions which is of crucial importance in every aspect.

Patients and Methods:

The data of 188 consecutive admissions with suspected diagnosis of acute coronary syndrome were analyzed retrospectively.

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 20-30 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. The pain was usually much longer in pts with Non-ST-elevation Myocardial Infarction (NSTEMI). The diagnosis of NSEMI required the confirmation of cardiac muscle necrosis by Cardiac Enzymes.

All Pts with suspected Non-ST-elevation Myocardial Infarction and most pts with UA were admitted to the Coronary care unit. Some pts with Unstable Angina were admitted to the intermediate care unit when the Coronary Care Unit 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 Non-ST-elevation Myocardial Infarction and UA during catheterization with possible intervention in the presence of a thrombus.

Coronary angiography was done, during hospitalization or soon after discharge.

Twenty-seven pts were excluded; ten had no or non-significant lesions and 17 pts with no Risk Factors. The remaining 161 patients were included in the analysis. They consisted of 102 pts with UA and 59 pts with NSTEMI.

Coronary Artery lesion was regarded significant if it cause >70% luminal narrowing. > 50% Left Main stem lesion was regarded equivalent to two main coronary arteries lesions.

RESULTS

The clinical data showed there were 54 pts with Single Risk Factor, 52 pts with two Risk Factors, 37 pts with three Risk Factors, 13 pts with four Risk Factors, and only 5 pts with five Risk Factors 1- Coronary lesions in Single Traditional Risk Factor (see table -1)

The Angiographic data showed that 31 out of the 54 pts with one Risk Factor had one or two discrete lesions affecting one main coronary artery. The remaining 23 pts had multiple lesions involving two or three main arteries. There were 132 lesions in the whole group. They were: 40 lesions in the 13 pts with Hyperlipidaemia; (3.1), 34 lesions in the 10 diabetics (3.4), 29 in the 10 Hypertensive pts (2.9), 21 in the 15 Smokers (1.4), and 8 lesions in the 6 pts with PFH (1.3)

The Data showed that eight out of the thirteen pts with Hyperlipidaemia (62%), and three out of the ten pts with Diabetes Mellitus (70%&) had multiple lesions involving at least two main arteries compared to 3 out of the 15 pts with Smoking (20%) and one of the six pts with PFH (17%. The multiple lesions took the form of diffuse disease involving at least a third of one main artery had occurred only in the Hyperlipidaemic pts and in the Diabetic pts; (23% and 20% respectively) but no Diffuse lesions were not reported in association with Smoking, PFH or HTN.

Data also showed that Coronary Artery Occlusion (Total or Subtotal) of at least one major artery had been reported in 38% of Hyperlipidaemics, 40% of diabetic, but such lesions were reported in 40% of the Smokers as well. In addition to that Smoking was the only Risk Factor where a coronary artery thrombus and coronary ectasia was detected (13% and 7% respectively).

Table 1 also showed that the lesions of the pts with hypertension were equally split between discrete lesion/s and multiple lesions with low incidence of total occlusions (10) but no diffuse disease.

Coronary Calcification was not reported in any pt. with single factor.

NOTE :-Please remember that we are talking about the coronary lesions that were associated with only one Risk Factor. Table -1- Coronary lesions in the 54 pts with Single Risk Factor.

M.R.F/ Lesion	Extent of stenotic lesions		P.V.	Diffuse Disease	Coronary occlusion	No. of lesions And average	Cor.. Throm bosis	Coro. Calcif- fication	Coronary Ectasia
	Discrete Lesions	Multiple Lesions							
Smoking 15 pts	12 80%	3 20%		Nil	6 40%	21 1.4	2 13%	Nil	1 7%
Hyperlip. 13 pts	5 38%	8 62%	0.03	3 23%	5 38%	40 3.1	nil	Nil	Nil

Diabetes Mellitus lOpts	3 30%	7 70%	0.02	2 20%	4 40%	34 3.4	Nil	Nil	Nil
Hyperten.. 10 pts	6 60%	4 40%	N.S	Nil	1 10%	29 2.9	Nil	Nil	Nil
Positive F.H 6 pts	5 83%	1 17%	N.S	Nil	nil	8 1.3	Nil	Nil	Nil

2- Coronary lesions in pts with two Risk Factors (see table -2-) There was 52 pts with two risk factors each. They included the following subgroups: -

1. Hyperlipidaemia (HL) - Diabetes Mellitus (D.M) 8pts.
2. Hyperlipidaemia (HL) - Hypertension (HTN 8 pt.
3. Hyperlipdaemia (HL) - Positive F.H 3 pts.
4. Hyperlipdaemia (HL) - Smoking) 10 pts.
5. SM-D.M. 5 pts.
6. SM - HTN 5 pts.
7. SM - PFH 3 pt.
8. D.M.-HTN 7 pts.
9. PFH - HTN 3 pts.

To assess the relationship of the five Risk Factors and the coronary artery lesions when two Risk Factors present in the same pt. we studied:-

A. The incidence of the various types of lesions in the pts associated with each of the Five Risk Factors and compared them with the incidence of that Risk Factor in the single Risk Factor group (see table - 2 -).:-

Comparing the rates of the coronary lesions that associated any isolated Risk Factor and when it was accompanied by another Risk Factor showed that those lesions had got worse in many aspects (see table -2-). The data showed that in pts with Smoking and those with PFH were associated with multiple lesions which had risen from 20% in the Single TRF group to 61% in the two Risk Factors group for pts with Smoking and from 17% to 45% for pts with PFH. Nevertheless the rates remained much behind the corresponding rates for Hyperlipidaemia and Diabetes Mellitus which had risen from 69% to 79% for the former and from 70% to 81% for the latter.

Likewise the rates of diffuse lesions in HL and D.M. had almost doubled; rising from 23% and 20% in the hyperlipidaemic and the Diabetic pts in the Single Risk Factor to 43% and 45% respectively in pts with two Risk Factors. On the other hand such lesions were not reported when HTN, Smoking, and PFH had occurred singularly but they appeared in rates of 45%, 26% and 11% respectively in the pts with those Factors when they were combined by a second Factor. Coronary artery thrombosis and coronary ectasia were not reported when Hyperlipidaemia and diabetes Mellitus were single Risk Factors but they appeared in the presence a second Risk Factor. On the other hand both types of lesions were reported when Smoking was a single Risk Factors and when it was combined with another Risk Factor but at the same rate. Coronary calcification, which had never been reported in association with any single Risk Factor, had appeared in both the Smoking group and the Hyperlipidaemia groups when they were combined.

Table -2- Comparison of the coronary lesions in each MRF when they were the only R.F i.e. Single R.F and when they were combined with another one ;two R.F.

T.R.F/ Lesion	Discre. lesions	Multiple lesions	Diffuse Disease	Occlusion	Thrombosis	Calcif-ication	Ectasia
Smoking Single Risk.F 15 pts	12 80%	3 20%	0	6 40%	2 13%	0	1 7%
Smoking two Risk Factors 23 pts	9 39%	14 P 61% 0.05	6 26% P.V=03	7 30%	3 13%	5 P 22% .V= 05	2 9%
HL. Single Risk Factor 13 pts	5 38%	8 62%	3 23%	5 38%	0	0	0
HL.in Two Risk Factor 28 pts	6 21%	22 79%	12 43%	10 34%	4 14%	5 18%	2 7%
D.M. Single Risk F. 10 pts	3 30%	7 70%	2 20%	4 40%	0	0	0
D.M. Two Risk Factor 21 pts	4 19%	17 81%	10 45%	10 48%	2 9%	0	2 9%
HTN Single Risk Factor 10 pts	6 60%	4 40%	Nil	1 10%	0	0	0
HTN two Risk Factor 23 pts	8 35%	15 65%	10 45% P.V=01	7 30%	1 4%	0	2 9%
PFH Single Risk Factor 6 pts	5 83%	1 17%	0	0	0	0	0
PFH two Risk Factors 9j)ts	5 55%	4 45%	1 11%	4 45%	0	0	0

B - Then we studied the lesions in each Subgroups of combined two Risk Factors and compared them with the other subgroups (see table -3-.

Unfortunately the number of pts in the subgroups was not large enough, however it is worthwhile looking at the Hyperlipidaemia subgroups which has relatively larger no. of pts :

1. Hyperlipidaemia and Smoking subgroup

Combined HL and SM was associated with a moderately high rate of multiple lesions {70%}, low rate of diffuse lesions (20%) and coronary occlusions (30%). The incidence of thrombosis was (30%.

2. Hyperlipidaemia and Diabetes Mellitus subgroup

This combination is associated with a very high rate of multiple lesions (88%). They had moderately high rate of total-subtotal (63%) and moderate rate of diffuse disease (50%). There was a low incidence of Coronary thrombosis (13%).

Comment about comparison : -

Admitting that the small number of pts in each group would weaken any conclusion however since the single Risk Factor data had shown that both HL and D.M were associated with predominance of multiple lesions and diffuse disease the two Risk Factors data showed that their combination were associated with a very high rate of multiple lesions reaching 88%, moderate rate of diffuse disease, and high rate of coronary occlusions.

Our Single Risk Factor data had shown that Smoking was associated more with discrete lesions and no diffuse disease . Its combination with HL ,the data showed, was associated with a moderately high Multiple lesions (70&) and low rate of diffuse disease and coronary occlusions .

Coronary thrombus was detected neither in HI nor in the D.M. when they were single factors but it was detected when Smoking was a single factor. After the combination Coronary thrombus was detected in both subgroups but the level in HL-SM subgroup was twice that in HL-DM subgroup.

3. Hyperlipidaemia and HTN subgroup

The combination was associated with high rate of multiple lesions and moderately high diffuse disease (86% and 71% respectively) but surprisingly there was no report of other lesions

Comment :-

This indicates that the general rule of deterioration of lesions when the number of Risk Factor increased is applicable to most but not all aspects of coronary lesions

Table -3 - Shows the coronary lesions distribution in the subgroups of pts with a pair of Risk Factors.

TRFs /Coron. Lesions	Discre. Lesions	Multiple lesions	Diffuse Diseas	Coron. Occlus.	Coronary Thrombus	Coron. Calcific.	Coronary Ectasia
HL -SM 10 pts	3 30%	7 70%	2 20%	3 30%	3 30%	5 50%	1 10%
HL-D.M 8 pts	1 13%	7 88%	4 50%	5 63%	1 13%	-	1 13%
HL-HTN 7 pts	1 14%	6 86%	5 71%	-	-	-	-
HL-PFH 3 pts	1 33%	2 67%	1 33%	2 67%	-	-	-
Hyperlipid. group 28 pts	6 21%	22 79%	12 43%	10 36%	4 14%	5 18%	2 7%
SM- HL 10 pts	3 30%	7 70%	2 20%	3 30%	3 30%	5 50%	1 10%
SM- D.M 5 pts	1 20%	4 80%	2 40%	2 40%	-	-	-
SM -HTN 5 pts	3 60%	2 40%	2 40%	2 40%	-	-	1 20%
SM -PFH 3 pt	2 67%	1 33%	-	-	-	-	-
Smoking group 23 pts	9 39%	14 61%	6 26%	7 30%	3 13%	5 22%	2 7%
D.M- HL 8 pts	1 13%	7 88%	4 50%	5 63%	1 13%	-	1 13%
D.M-HTN 8 pts	2 25%	6 75%	3 38%	3 38%	1 13%	-	1 13%
D.M-SM 5 pts	1 20%	4 80%	2 40%	2 40%	-	-	-
Diabetes group 21 pts	4 19%	17 81%	9 43%	10 48%	2 9%		2 9%
HTN-HL 7 pts	1 14%	6 86%	5 71%	-	-	-	-
HTN D.M 8 pts	2 25%	6 75%	3 38%	3 38%	1 13%	-	1 13%
HTN -SM 5 pts	-> 60%	2 40%	2 40%	2 40%	-	-	1 20%
HTN-PFH 3 pts	2 67%	1 33%	-	2 67%	-	-	-
Hypertension group 23 pts	8 35%	15 65%	10 45%	7 30%	1 4%		2 9%

PFH -HL 3 pts	1 33%	2 67%	1 33%	2 67%	-	-	-
PFH-SM 3 pt	2 67%	1 33%	-	-	-	-	-
PFH-HTN 3 pts	2 67%	1 33%	-	2 67%	-	-	-
Positive FH group 9 pts	5 55%	4 45%	1 11%	4 45%	-	-	-

Coronary Lesions in pts with Three Risk Factors (see table 4)

There were nine subgroups of pts the 37 pts with three Risk Factors each. They were;-1 - 17 pts with HI, D.M, and HTN,

2- 2 pts with HL, D.M,, and PFH
3- 3 pts with HL, HTN, and PFH
4- 3 pts with HL, SM, and PFH
5- 3 pts with HL. SM, and D.M
6- 3 pts with HL SM, and HTN
7- 3 pts with SM, D.M., and HTN
8- 2 pts with SM, HTN, and PFH,
9- 1 pt with SM, D.M., and PFH,

The occurrence of three Risk Factors in the same pt makes it hard to study the separate effect of each Risk Factor on the coronary lesions .In addition to that the number of pts in each subgroup, apart from one, were too small to allow meaningful comparison. Only one subgroup ie Hyperlipidaemia, Diabetes Mellitus, and Hypertension which included the largest no. of pts and it is worthwhile studying .

This Subgroup included seventeen pts. The angiographic data showed deterioration of most parameters of severity of the lesions. Out of the 17 pts only two had discrete lesions (12%). The remaining 15 pts had multiple lesions (88%). Two fifths of pts had diffuse disease while more than half of them had Total/Subtotal occlusions (53%).

Table 4 showed that the incidence of multiple lesions and diffuse disease in the HL group-2, D.M group 2, and the HTN-2 group were marginally higher than the corresponding level of pts with two Risk Factors. Remarkably there was a mild decline of multiple lesions associated with Smoking where it dropped from 61% when Smoking was combined by one Risk Factor to 53% here. This may reflect the consistent finding in this study of the association of Smoking with less extensive disease however other parameters of deterioration such Diffuse Disease, coronary occlusion, and thrombosis had worsened.

Table -4- Types of lesions in 37 pts with three Risk Factors.

MRF/ Lesion	Discrete lesions	Multiple lesions	Diffuse Disease	C Occlu sion	C.Thro-mbosis	C. Calci-fication	C. Ectasia
SM group 2 15 pts	7 47%	8 53%	6 40%	8 53%	4 27%	1 7%	1 7%
HL grroup 2 30 pts	5 17%	25 83%	14 47%	13 43%	1 3%	5 17%	1 3%
DM group 2 27 pts	4 15%	23 85%	13 48%	11 41%	2 7%	4 15%	2 7%
HTN group 2 28 pts	6 21%	22 79%	11 39%	12 43%	2 7%	4 14%	3 11%
PFH group 2 11 pts	5 45%	6 55%	2 18%	4 36%	0	1 9%	0

Discussion

Though the concept of Cardiovascular Risk Factors has formally long existed the direct link between the risk factors, notably hypertension and hypercholesterolemia, and atherosclerosis required series of prospective epidemiological and clinical studies to substantiate it (5.6, 7, 8, and 9). As a matter of fact doubt has lingered regarding the role of cholesterol until surprisingly recently when many pharmacological interventional studies confirmed the cause and effect relation (10, 11, 12, and 13). However to what extent these Risk Factors influence the various types' lesions of atherosclerosis is under exploration.

This study had addressed a very important issue and it seems that much larger number sample of pts is necessary however some figure in the seemed to carry worthwhile message.

This study has Shown, when we deal with patients with only one risk factor, Smoking and Positive Family History for Ischaemic Heart Disease appeared to be associated with less extensive lesions than those associated HL. Chen et al found that Smoking and PFH were more prevalent in young pts with I.H.D who were found to have milder coronary disease involving one coronary artery only (14).In our study the association between Smoking or Positive Family History of I.H.D. and the occurrence of less severe lesions has

no age limit though most of patients were younger than 55 years. Angeja etal from the University of California also found that Smokers had milder disease than the others. (15)...

Diabetes Mellitus is a well known predisposer to diffuse and multiple lesions (16).In our study Diabetes mellitus was associated with multiple lesions involving two arteries in half of the pts. Although the incidence of Multiple lesions in two arteries were less in Hypertension than Diabetes Mellitus however the finding in this study that hypertension was associated with higher no. of lesions than Diabetes Mellitus was most surprising. Nevertheless Hypertension unlike Diabetes mellitus is not associated with diffuse lesions.

This study showed that Smoking was associated with coronary artery thrombus in a fifth of the pts. This is a crucial finding since Smoking has been reported to be associated with increased thrombogenesis and myocardial infarction (17,1 this study had shown that combination of two Risk Factors was associated with worsening of coronary lesions in away that may exaggerate some if not most of original features of the combined factors. Smoking was associated with low incidence of multiple lesions while hyperlipidaemia is associated with high incidence of multiple lesions. The study showed that combining the two Factors would be associated with moderate incidence of multiple lesions. Smoking is associated with coronary thrombi in one fifth of the'pts. While no such association with Hyperlipidaemia. The study had shown that Combining Hyperlipidaemia and Smoking was associated with coronary thrombi in nearly a third of the pts. Gyongyosi M etal found an association between hyperlipidaemia, Smoking and higher frequency of thrombus (19). On the other hand combining HI and D.M., which was found in our study to be associated with high incidence of multiple lesions for Hyperlipidaemia and modest incidence in case of Diabetes Mellitus with low rate of diffuse disease for both, has resulted in a very high rate of multiple lesions and moderate rate of diffuse disease.

Conclusion: As single Risk Factor Diabetes Mellitus and hyperlipidaemia, compared to Smoking, were significantly associated with multiple lesions and diffuse disease. Smoking seemed to be associated with coronary thrombosis as well as coronary occlusion. Increasing the no of the MRF was associated with worsening of the coronary lesions though such deterioration was less pronounced in the presence of Smokiog

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