Sudden Death from Coronary Heart Disease*

Survival Time, Frequency of Thrombi, and Cigarette Smoking

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An autopsy study on the number of recent coronary thrombi present in sudden and unexpected fatalities from coronary heart disease again reveals their infrequent occurrence. Also, it is shown that there is an increase in the frequency of recent coronary thrombi with increasing survival time from the onset of the acute coronary heart attack. This tends to support the concept that recent coronary thrombi, when found in these acute events, do not usually trigger the onset of the attack but develop as a secondary phenomenon during the course of the acute event. Furthermore, cigarette smoking was noted not only to have an exceptionally close statistical correlation with these sudden acute coronary deaths, but also appeared to be associated with a shorter survival time of these acute episodes. The nature of the autopsy population from which these cases were selected dictates caution in generalizing to the population at large.

It is estimated that about 25 percent of all deaths from acute myocardial ischemia as a result of coronary atherosclerosis are sudden and unexpected and usually occur within one hour of the clinical onset of the initial "attack." There are approximately 500,000 deaths in the United States every year from acute myocardial infarction and it appears that about 50 percent die before adequate medical care is available. In the sudden cases, the events are so rapid that there are no physicians in attendance and the deaths occur before hospitalization is possible. In an attempt to prevent some of these deaths, mobile coronary care units have been developed in a few areas in order to get to the scene of the "heart attack" as soon as possible. These units are equipped and staffed to provide all the necessary resuscitative as well as medical and electrical anti-arrhythmic therapy. To give the most rational treatment in these situations, it has become essential to understand with greater precision the underlying mechanisms, the pathogenesis, and the circumstances involved in the earliest phases of these acute episodes. It is also important to know more about the environmental factors which may influence the precipitation and aggravation of these acute clinical events of myocardial ischemia.

In 1961 we reported that the frequency of fresh coronary thrombi in these sudden and unexpected deaths from coronary heart disease was approximately 20 percent. The other 80 percent did not reveal any recent thrombi but had advanced coronary atherosclerosis which significantly reduced the lumen diameter in at least one site. Also it was noted that the frequency of recent coronary thrombi was related to the duration of survival from the onset of the obvious clinical manifestations of the acute episode. Fresh coronary thrombi were found in 49 (16 percent) of 303 cases surviving 1 to 24 hours and in 100 (54 percent) of 200 cases surviving over 24 hours.

At least four possible explanations have been offered to account for these autopsy findings. The first of these is that the increased frequency of recent thrombi seen with longer survival may be an artefact caused by the postmortem lysis of some of these freshly formed thrombi as a result of an excessive production of fibrinolysins during the...
agonal state. Currently there is no direct method of unequivocally excluding this possibility. However, most of the available evidence tends to exclude artefact as an adequate explanation. For instance, postmortem examination of the coronary arteries in these cases of acute coronary deaths most often reveals that the major coronary arteries in the cases without definite thrombi are completely free of blood or bloody material. If some of these fresh thrombi had been recently lysed immediately post-mortem one would expect to find at least in a few instances a partially liquified blood coagulum or a remnant of thrombi within the lumen of a major coronary artery. These have not been demonstrated. A careful study with meticulous dissection has shown that over 40 percent of the patients with acute myocardial infarcts who died in the hospital did not contain any recent thrombi in the major coronary arteries. In the nonthrombotic cases, the infarcts were of the multifocal subendocardial type. In the presence of thrombi, the infarcts were unifocal or transmural. It is unlikely that post-mortem lysis of thrombi could be so selective as to only liquify those thrombi that allegedly might have been present in the cases with subendocardial infarcts and not lyse those thrombi that were associated with transmural infarcts. On several occasions, it has been possible to perform autopsies on cases of acute coronary deaths within 15 minutes of the fatality. In none of these instances was there any evidence of recent infarct or partially lysed thrombi. It is also unlikely that an artefact which in a sense occurs by chance could account for identical percentages of thrombi being present in separate studies carried out almost a decade apart (our previous study and this current report).

A second possible explanation is that the coronary arteries were not examined with sufficient care so that some thrombi, though actually present, were not observed. The coronary arteries were examined according to standardized techniques specifically designed for the purposes of finding thrombi and the method of examination and care exercised were similar in each case regardless of the duration of survival. Also the findings of a similar overall percentage of thrombi in other medical examiners' offices would tend to rule out this explanation.

A third proposition is that the cases with coronary thrombi are the ones with the best prognosis for survival. This explanation is easily negated by the fact that the cases with thrombi have the more extensive infarction.

Finally there is the explanation that coronary thrombi usually do not initiate the acute clinical episode but may develop early in the course of the attack as a consequence of certain events which favor their formation. The newly formed thrombus then intensifies the ischemia and increases the severity of the attack and its consequences.

Among the environmental factors thought to be associated with the precipitation or influencing the course of an acute episode of ischemia are cigarette smoking and physical activity. This study concerns itself only with cigarette smoking. There are numerous reports showing a close association between cigarette smoking and a higher incidence of angina and myocardial infarction. Also a recent study demonstrated an even closer association between heavy cigarette smoking and sudden acute fatal coronary heart attacks.

This paper reports a new study on the incidence of recent thrombi as related to the duration of survival from the onset of the "attack" and the possible influence of cigarette smoking on the length of survival and the frequency of these events.

**METHODS**

The subjects were derived from consecutive autopsies on men who died relatively suddenly and unexpectedly from seemingly first acute clinical episodes of CAHD. There were 186 such autopsies which included events that were witnessed or unwitnessed and also included nonsmokers, former smokers, cigar and pipe smokers and cigarette smokers.

The diagnosis of coronary heart disease as the cause of death was based on the following considerations:

1. In the witnessed cases, the sudden onset of chest pain in an apparently asymptomatic patient that terminated fatally within a relatively short period of time.
2. The presence of varying degrees of advanced atherosclerosis with at least one segment of occlusion compromising at least 70 percent of the lumen diameter in a major coronary artery.
3. The absence of any other significant morphologic alterations or history that could reasonably account for the symptoms and death.

Unwitnessed cases required obviously only criteria 2 and 3. The presence of a recent thrombus in a major coronary artery is helpful but not essential for a diagnosis. In the witnessed cases an estimate of the time from the clinical onset to death was recorded. These were then classified into those patients who died in less than one hour from the onset and those who survived from one to eight hours. An additional 100 autopsied cases of men who died from acute myocardial infarction at Brookdale Hospital Center were utilized for the group that survived more than eight hours.

The hearts were examined with a standardized technique designed for the purpose of evaluating the degree of coronary atherosclerosis and the presence of fresh thrombi. Cross sections were made of all major coronary arteries at intervals of 2 to 3 mm. The myocardium was examined for any evidence of recent or old infarction. Histologic studies were utilized whenever required.

The smoking habits of the deceased individuals were determined by questionnaires sent to the closest living relatives. Only those responses were utilized in which it appeared
**Table 1—Frequency of Recent Coronary Thrombi in Sudden Deaths* From CAHD As Related to Smoking Habits**

<table>
<thead>
<tr>
<th>Smoking Habits</th>
<th>No. Subjects</th>
<th>No. with Recent Thrombi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmokers</td>
<td>57</td>
<td>15 (26.0%)</td>
</tr>
<tr>
<td>Smokers</td>
<td>132</td>
<td>21 (15.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>189</td>
<td>36 (19.0%)</td>
</tr>
</tbody>
</table>

*Includes unwitnessed cases.

that the informant had sufficient knowledge to give a valid smoking history. The questionnaire was deliberately kept as simple as possible and was limited to the following questions:

1. Did the deceased smoke cigarettes?
2. Did he smoke less than 50 cigarettes per day?
3. Did he smoke more than 50 cigarettes per day?
4. Had he stopped smoking, and if so, when?
5. Did he smoke a pipe or a pipe?

Other data recorded were age, race, previous illness, occupation, and place of residence. The autopsy observations were determined and recorded without prior knowledge of any of the above data.

**FINDINGS**

In the total group of subjects, the frequency of recent thrombi was 19 percent (see Table 1). This included the witnessed and unwitnessed cases and all categories of smoking habits as well as those who survived more than one hour. In the nonsmokers this was 26 percent and in the smokers it was 15.9 percent. In 102 of the 189 cases, there were reliable witnesses to the acute episodes who were able to give reasonable accounts of onset and length. In most cases, death occurred in less than 30 minutes. In order to minimize overlap, the cases were divided into those that survived less than one hour and those that survived between one and eight hours. The hospital autopsies consisted of the more than eight-hour survivors. The frequency of coronary thrombi increased from 17.5 percent to 36.4 percent as survival time increased from less than one hour to more than one hour, and increased still more to 57 percent when survival extended beyond eight hours (see Table 2). When this was related to smoking habits (see Table 3), survival time decreased in the heavier smokers so that only 5 percent of this group survived beyond one hour, whereas, 33 percent of the nonsmokers survived more than the one hour. This close association between cigarette smoking and sudden death from CAHD is even more striking (see Table 4) under the age of 50 when one compares the ratio of nonsmokers to smokers. However, the association was less evident within the older ages presumably because of the large number of the deaths from coronary heart disease in the cigarette smoking group at the younger ages. For every nonsmoker under the age of 50 who died suddenly and unexpectedly from coronary heart disease, there were 16 such deaths in those who smoked more than one pack of cigarettes per day. The significance of this ratio is evident when it is realized that in the Medical Examiners' autopsied population under study (includes all type of cases, accidents, etc.) that for each nonsmoker there were only 1.3 more than one pack per day cigarette smokers.

**DISCUSSION**

The current findings of an increase in frequency of coronary thrombi with an increase in duration of survival from the onset of the clinical manifestations of the coronary heart attack are almost identical with those of the study reported in 1961.2 Regardless of the interpretation of these findings, the fact that the results are identical in studies performed almost ten years apart would support the validity of

**Table 2—Frequency of Recent Coronary Thrombi As Related to Duration of Survival**

<table>
<thead>
<tr>
<th>Survival Time</th>
<th>All Subjects</th>
<th>No. with Recent Thrombi</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hour</td>
<td>80</td>
<td>14 (17.5%)</td>
</tr>
<tr>
<td>1 to 8 hours</td>
<td>22</td>
<td>8 (36.4%)</td>
</tr>
<tr>
<td>&gt;8 hours*</td>
<td>100</td>
<td>57 (57.0%)</td>
</tr>
</tbody>
</table>

*This group of cases were not from the Medical Examiner's office, but were from autopsies at the Brookdale Hospital Center.

**Table 3—Survival Time from Onset of Acute "Attack" and Smoking Habits**

<table>
<thead>
<tr>
<th>Smoking Habits</th>
<th>All Subjects</th>
<th>Survived Less than 1 Hour</th>
<th>Survived 1-8 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmoker</td>
<td>18</td>
<td>12</td>
<td>6 (33.3%)</td>
</tr>
<tr>
<td>Less than 1 pack</td>
<td>30</td>
<td>22</td>
<td>8 (26.6%)</td>
</tr>
<tr>
<td>More than 1 pack</td>
<td>40</td>
<td>38</td>
<td>2 (5.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>88</td>
<td>72</td>
<td>16 (18.2%)</td>
</tr>
</tbody>
</table>

**Table 4—Ratio* of Smoking Habits in Sudden Deaths from CAHD (102 Males)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Nonsmoker</th>
<th>Less than 1 Pack</th>
<th>More than 1 Pack</th>
</tr>
</thead>
<tbody>
<tr>
<td>51 to 60</td>
<td>1</td>
<td>4.0</td>
<td>16.0</td>
</tr>
<tr>
<td>60</td>
<td>1</td>
<td>2.5</td>
<td>6.0</td>
</tr>
<tr>
<td>Ratio in all male</td>
<td>1</td>
<td>0.8</td>
<td>1.3</td>
</tr>
</tbody>
</table>

*Ratio indicates the number of light and heavy smokers for each non-smoker at various age levels.
these observations. The concept that some mechanism other than that the formation of a new thrombus triggers the onset of many coronary heart attacks is again restated and that it is during the early phases of this "attack," in progress, that arrhythmias or metabolic deficiencies in the myocardium disturb the hemodynamics of an already embarrassed coronary circulation to favor the formation of a thrombus in a vessel previously compromised by atherosclerosis. This additional obstruction to the circulation enhances the ischemia sufficiently to now produce a transmural infarct which otherwise might not have developed. With increasing time of survival and with the persistence of a myocardial metabolic disturbance and arrhythmia, there is a greater opportunity for such thrombi to develop. In this connection it is pertinent to note that in an experimental study on calves the induction of prolonged ventricular fibrillation was accompanied by massive subendocardial damage. No thrombi were present and the severity of the myocardial lesions increased with the duration of the experiment.

With presently available autopsy techniques it is difficult if not impossible to obtain additional information for further support for the concept of the secondary origin of many coronary thrombi. Autopsies unfortunately provide only one still picture of a process which during life is rapidly evolving, changing, and dynamic. The cause often cannot be distinguished from effect. If there is to be confirmation or rejection of this concept it may have to await the time when there will be enough cases from the mobile coronary care unit experiences, who have been treated within the first 30 minutes of the onset of the attack and who have survived for a sufficient length of time. It will then be possible to determine whether these survivors reveal greater or lesser numbers of transmural infarcts than anticipated from experience previously. A significant decrease in this type of infarct which is usually associated with coronary thrombi would contribute important support for the concept of a secondary development of the thrombus after the onset of the attack. This would provide early encouragement for intervention in an attempt to interrupt those processes favoring the formation of thrombi.

The findings also support the view that cigarette smoking exerts some if not its major harmful effects on the acute clinical event rather than on the chronic atherogenic process. The fact that fewer coronary thrombi were present in the more than one pack per day cigarette smokers can be explained by the observation that these are the very cases with the shortest survival and the number of thrombi are noted to increase with longer survival.

The cases in this study were drawn from an overall group of 500 consecutive Medical Examiner autopsies. The smoking history questionnaires had been sent to the next of kin in all of these cases. There were 60 percent respondents. However, the age distribution, sex ratio and causes of death were similar in the autopsies with respondents and nonrespondents. The frequency of coronary thrombi and duration of survival from onset of "attack" were also similar in the respondent and nonrespondent groups. The smoking patterns of the Medical Examiner population as whole in the respondent group showed a ratio of 1 nonsmoker to 1.3 more than 20 cigarettes per day smokers. The ratio in the population from which the Brookdale Hospital autopsies were drawn was 1 nonsmoker to every 1.4 more than 20 cigarettes per day smokers. However, it should be noted that no smoking comparisons were made in the study with the group that survived more than eight hours. Unfortunately, the nature of the problem precludes sufficient numbers of more than eight hour survivors from a Medical Examiner case study as they are admitted to the hospital and therefore upon death do not become Medical Examiner cases. At any rate, the selected population upon which this study was of necessity based, precludes the unconditional generalization of these findings to the population at large.

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