

# FOCAL AND DIFFUSE PAPILLARY MUSCLE FIBROSIS AND SMALL VESSEL SCLEROSIS OF THE HEART

A CLINICAL-PATHOLOGIC STUDY OF 375 AUTOPSIES

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乳頭筋線維症と小血管硬化症

剖検 375 例の臨床的病理学的検討

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国立予防衛生研究所 - 原爆傷害調査委員会

JAPANESE NATIONAL INSTITUTE OF HEALTH OF THE MINISTRY OF HEALTH AND WELFARE

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HIROSHIMA AND NAGASAKI, JAPAN

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#### SUMMARY

A retrospective clinical-pathologic study was made of papillary muscle fibrosis and small vessel sclerosis of the heart in 375 autopsies from the ABCC-JNIH Adult Health Study sample in Hiroshima and Nagasaki. The histopathologic findings were correlated with clinical diagnoses which included hypertension, hypertensive heart disease, myocardial infarction, and diabetes mellitus.

Two distinct types of fibrosis, diffuse and focal, were observed in the papillary muscles of the heart. The diffuse type was present in almost half of the autopsies, was associated with sclerosis of the small vessels of the papillary muscles and with hypertension but was not related to clinical cardiac disease or to diabetes mellitus. The focal type of papillary muscle fibrosis was related to coronary heart disease, myocardial infarction and cardiac hypertrophy but not to sclerosis of small vessels or diabetes mellitus. There was no evidence that any of these changes were related to prior radiation exposure at the time of the atomic bomb.

#### INTRODUCTION

Chronic vascular and ischemic changes in cardiac papillary muscles are important to an understanding of ischemic heart disease and cardiac changes

#### 要約

広島・長崎のABCC-予研成人健康調査対象者中の剖検375例について、心臓における乳頭筋線維症ならびに小血管硬化症に関する遡及的臨床的病理学的検討を行った。組織病理学的所見と高血圧、高血圧性心疾患、心筋硬塞症および糖尿病などの臨床診断との相関関係を調べた。

心臓の乳頭筋に瀰漫型および限局型の2種類の明確な線維症が認められた。瀰漫型線維症は剖検例のほぼ半数に存在し、乳頭筋小血管硬化症および高血圧と関連があったが、臨床的な心疾患や糖尿病とは関連がなかった。限局型の乳頭筋線維症は冠動脈性心疾患、心筋硬塞および心臓肥大と関係があったが、小血管硬化症や糖尿病との関係は認められなかった。これらの変化が原爆時の放射線被曝と関係があるという証拠は全くなかった。

#### 緒言

心臓の乳頭筋における慢性的な血管変化および虚血性変化は、虚血性心疾患や加齢と関係ある心臓変化を理解

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related to aging.<sup>1-4</sup> Although there are some conflicting opinions, most reports indicate that there is little or no relation between the degree of atherosclerosis of the major coronary arteries and their intramural branches.<sup>3-7</sup> Very extensive sclerosis of large branches of the coronary arteries may be present with little or no involvement of the intramural vessels. The atheromatous lipid-containing lesions of the epicardial arteries end abruptly at the point of entry into the myocardium.<sup>6,8</sup> Widespread arteriolar sclerosis associated with marked and persistent hypertension may be present in other organs without involvement of the intramural vessels of the heart, and the small myocardial vessels often show age-related sclerotic changes in the absence of small vessel sclerosis elsewhere.<sup>6,9</sup> Similar age-related intramural vascular changes are reported to occur frequently in dogs and other animals.<sup>5,10</sup> In man, these changes are said to be more prominent in the distal segments of the vessels, especially those in the papillary muscles, which vary in diameter from 50 to 400 $\mu$  and have a definite media and internal elastic lamina.<sup>2,3</sup>

The distribution of the intramural branches of the coronary arteries has been investigated extensively. Estes et al,<sup>11</sup> using injection methods, reported that there are two types of intramural vessels. Type A vessels divide soon after entering the myocardium and send branches to the tethered type of papillary muscle.<sup>2</sup> Type B vessels penetrate to the subendocardial layer where they form multiple anastomosing arcades and also supply the papillary muscles. Baroldi and Scomazzoni<sup>12</sup> found numerous anastomotic and ramifying branches at all levels of the heart varying in diameter from 20 to 350 $\mu$  or more as well as a rich subendocardial network. Ranganathan and Burch<sup>13</sup> reported that papillary muscle artery distribution is related to the type of muscle; well developed finger-like papillary muscle receives a large central artery which extends to the muscle apex with few or no anastomoses, and the tethered type of papillary muscle has a segmental distribution of long penetrating intramural vessels. A mixed type of arterial supply is also present in some cases. No reports were found to indicate that the type of vascular distribution is related to the degree of vessel sclerosis.

Pathologic alterations of the intramural vessels vary considerably but the lipid associated changes of atherosclerosis are not seen. Observed findings include thickening of walls with intimal hyperplasia, subintimal fibrosis, hyaline degeneration, fibroelastosis, medial fibrosis, splitting of the elastica, intimal elastic hyperplasia, fusion of intima and media, atrophy of muscle, adventitial fibrosis, and fusiform thickening.<sup>3,7,14,15</sup> It is not clear whether

する上に重要である。<sup>1-4</sup> 相反する意見も若干あるとはいえ、ほとんどの報告は、主要冠状動脈とその心壁内動脈枝におけるアテローム性動脈硬化症の程度の間に関係がほとんど、または、全くないことを示している。<sup>3-7</sup> 冠状動脈の主要動脈枝に極めて広範の硬化症があっても、心壁内血管に変化がほとんど、または、全くない場合がある。心外膜の動脈におけるアテローム性脂質含有病変は、心筋層への進入点で急に終わることが認められている。<sup>6,8</sup> 顕著な持続性高血圧に関連してその他の各臓器に広範囲の細動脈硬化症があっても、心壁内血管に変化がないこともあり、一方、他の部位に小血管硬化症がなくても、心筋における小血管に年齢に関係ある硬化性変化がしばしば認められる。<sup>6,9</sup> 年齢に関係ある同じような心壁内血管変化が、イヌやその他の動物にもしばしば起こると報告されている。<sup>5,10</sup> ヒトにおいては、これらの変化は血管の末端部、特に直径が50ないし400 $\mu$ であり、明確な中膜と内弾性板を有する乳頭筋の血管において、より顕著であるといわれている。<sup>2,3</sup>

冠状動脈の心壁内動脈枝の分布について多くの研究がある。Estesら<sup>11</sup>は、注射法を使用して2種類の壁内血管があると報告した。A型血管は心筋層内に進入した直後に分岐し、分枝は連鎖型の乳頭筋へ走る。<sup>2</sup> B型血管は、心内膜下層まで貫通し、そこで互いに吻合する分枝に分かれて乳頭筋へ血液を供給する。BaroldiおよびScomazzoni<sup>12</sup>は、心内膜下における豊富な血管網のほかに、心臓の各層に径20 $\mu$ から350 $\mu$ 以上に及ぶ多数の吻合枝や分枝を認めている。RanganathanおよびBurch<sup>13</sup>は、乳頭筋における動脈の分布は、その筋の種類があると報告した。すなわち、よく発達した指状型の乳頭筋は大きな中心動脈を受け、それはほとんど、または、全く吻合を示すことなく筋の先端部まで走る。また、連鎖型の乳頭筋は、心壁内における長い貫通枝の分節状分布を受ける。若干例では混合型の動脈分布もみられる。血管分布の型式が血管における硬化症の程度に関係があることを示す報告はない。

心壁内血管における病理学的変化は多種多様であるが、アテローム性動脈硬化症の脂質に関連した変化はみられない。観察されている所見には、内膜過形成を伴う血管壁の肥厚、内膜下線維症、硝子変性、線維弾力線維症、中膜線維症、弾力層の分裂、内膜の弾力線維過形成、内膜と中膜の癒合、筋肉の萎縮、外膜の線維症および紡錘状肥厚がある。<sup>3,7,14,15</sup> 同一の組織切片において、1種

all of these changes represent a single type of sclerosis although it is common to find more than one kind of alteration in the same histologic section.

Three distinct types of ischemic change of the papillary muscles have been described. The first, massive infarction of papillary muscle, sometimes with rupture, leads to acute incompetence or tenting of the mitral valve. This is an infrequent but dramatic occurrence which has serious clinical implications.<sup>2,16</sup> It is not considered in this study. The second, named focal fibrosis by Brand et al,<sup>4</sup> is more frequent and consists of fibrosis of the papillary muscle usually associated with a transmural or subendocardial infarct of the left ventricle.<sup>3,4</sup> It occurs in 20% to 50% of hearts with acute myocardial infarcts. When healed and replaced by fibrosis, the papillary muscle presents a characteristic picture of sharply demarcated scar tissue separated from the endocardial surface by a layer of surviving muscle fibers. Thin-walled vessels often persist in the midst of the fibrous scar and may also be surrounded by surviving muscle fibers. The third type of ischemic papillary fibrosis, called diffuse by Brand et al,<sup>4</sup> extends to the endothelial surface without retention of an interposed layer of surviving muscle.<sup>3,4</sup> Although vessels at the margins of these fibrotic areas are often sclerotic, this diffuse type of papillary muscle fibrosis is not associated with atherosclerosis of the major coronary arteries, myocardial infarction, cardiac hypertrophy, or hypertension. Both the diffuse type of fibrosis and sclerosis of the small vessels of the papillary muscles are more frequent in older persons. They have been found in 25% to 60% of hearts in consecutive autopsy series.<sup>17</sup> Diffuse and focal fibrosis, although apparently unrelated, may occur together. Brand et al,<sup>4</sup> found either focal or diffuse fibrosis or both in 80% of their cases. It is a curious paradox that whereas there is often little involvement of papillary arteries in the focal type of papillary muscle fibrosis which is associated with ischemic heart disease, there is extensive papillary artery sclerosis in the diffuse type of papillary muscle fibrosis which is not associated with coronary atherosclerosis or myocardial infarction.

A clinical-pathologic study based on 375 autopsies performed at ABCC in Hiroshima and Nagasaki provided an opportunity to investigate these vascular and fibrotic changes in the myocardium and papillary muscles. This is a report of the changes and relationships observed.

## METHODS AND MATERIALS

The JNIIH-ABCC Life Span Study (LSS) sample selected in Hiroshima and Nagasaki for the study of

類以上の変化を認めるのが通例であるが、これらの変化がすべて単一種類の硬化症の表現であるかどうかは明らかでない。

乳頭筋には3種類の虚血性変化が記述されている。その一つは、乳頭筋の広汎硬塞であり、これは時々破裂を伴い、僧帽弁の急性不全またはテント状化をもたらす。これは、まれではあるが、劇的な発症であって、临床上重大な意味を有するものである。<sup>2,16</sup> 今回の研究ではこの変化は考慮しなかった。第2の変化は、Brandら<sup>4</sup>によって限局型線維症と呼ばれたものであり、これはより高頻度に見られ、この乳頭筋線維症は左心室の経壁性、または、心内膜下硬塞に伴って起こることが多い。<sup>3,4</sup> 急性心筋硬塞のある心臓の20%から50%にこの変化が発現する。治癒して線維症で置き換えられた場合、乳頭筋は、残存筋線維層によって心内膜表面から隔てられた境界の鮮明な癒痕組織の特徴的な像を示す。壁の薄い血管が線維性癒痕の中に残存していることがしばしばあり、その周囲に残存筋線維がみられることもある。乳頭筋における第3の虚血性線維症は、Brandら<sup>4</sup>によって瀰漫型と呼ばれたものであり、残存筋肉層の介在がなく、内皮表面まで及ぶ。<sup>3,4</sup> この種の線維化領域の辺縁部における血管は硬化症を呈することがしばしばであるが、この瀰漫型の乳頭筋線維症は、主要冠状動脈のアテローム性動脈硬化症、心筋硬塞、心臓肥大または高血圧との関連はない。乳頭筋における瀰漫型線維症および小血管硬化症はともに高齢者に多い。連続剖検例において心臓の25%から60%にこの変化が認められている。<sup>17</sup> 瀰漫型および限局型の線維症は、互いに無関係であるように思われるが、その併発がみられることもある。Brandら<sup>4</sup>は、限局型または瀰漫型の線維症のいずれか一方あるいはその両方を被検例の80%に見ている。虚血性心臓疾患に関連して発生する限局型の乳頭筋線維症では、乳頭筋における動脈にほとんど変化がないことが多いのに対して、冠状動脈のアテローム性動脈硬化症または心筋硬塞とは関連のない瀰漫型の乳頭筋線維症では、乳頭筋に広範囲な動脈硬化症があるのは奇妙な逆説である。

広島・長崎におけるABCCで実施された剖検375例に基づく臨床的・病理学的検討を通じて心筋および乳頭筋におけるこれらの血管変化および線維症変化を調べる機会を得た。観察した変化および関係について報告する。

## 方法と材料

原爆被爆者および非被爆対照者における放射線の遅発性影響を調査するために広島および長崎において選択され



delayed radiation effects in A-bomb survivors and nonirradiated controls includes a subsample, the ABCC-JNIH Adult Health Study (AHS) sample, chosen for biennial clinical surveillance and evaluation. The physical examinations were begun in 1958 and are presently in their 9th cycle. The details of selection for the sample and the various clinical examinations have been described.<sup>18</sup>

During the period, 1965-70 (Hiroshima) and 1968-70 (Nagasaki), 375 postmortem examinations were performed at ABCC on members of the AHS sample most of whom had been examined at least once before death. In most instances the last examination occurred more than 6 months before death. Therefore, the clinical-pathologic study was directed at healed changes which might have been present and might have had clinical associations during the last physical examination.

The clinical evaluation was based on the records of the biennial examinations without knowledge of autopsy findings or radiation exposure status. In some instances the history of the terminal illness was also available. The clinic charts were reviewed for evidence of heart disease, hypertension, and diabetes mellitus. All available electrocardiograms were reexamined and coded according to the ABCC clinical and WHO codes.<sup>19,20</sup> Electrocardiographic evidence of myocardial infarction included codable QRS abnormalities, ST-T changes suggestive of subendocardial infarction and temporal changes on sequential tracings. These were coded as definite or possible based on the divisions of the ABCC clinical code.<sup>19</sup> The criteria for possible and definite hypertension, hypertensive heart disease, and diabetes mellitus are described in Appendix A.

Permission for autopsy was sought by autopsy contactors who were unaware of the clinical diagnoses. All autopsy diagnoses were reviewed and coded for principal cause of death. The degree of atherosclerosis of the proximal 5 cm of each of the three major coronary arteries was evaluated by the American Heart Association panel method modified in that, regardless of size or extent, areas of narrowing or obstruction of the lumen determined the reading for the entire vessel.<sup>21-23</sup> The highest atherosclerosis score recorded was used for correlation with other observations.

At least seven blocks of tissue were taken from each heart. The first four, approximately at the junction of the middle and upper thirds of the ventricles and parallel to the base of the heart, included 1) anterior septum with adjacent anterior portions of both ventricles, 2) anterolateral left ventricle including the anterior papillary muscle,

ている予研-ABCC寿命調査集団の中には、2年ごとの臨床的観察と評価が目的で選ばれたABCC-予研成人健康調査集団と呼ばれる副次群が含まれている。その診察が開始されたのは1958年で、現在第9診察周期に入っている。調査集団の選択法および種々の臨床検診の詳細についてはすでに報告されている。<sup>18</sup>

広島では1965-70年、長崎では1968-70年の期間に成人健康調査集団中の死亡者375人の剖検が実施されたが、その大部分は生前に少なくとも1回受診している。大抵の場合、最終検診が実施されたのは死亡の6か月以上も前であった。したがって、今回の臨床的・病理学的検討は、最終診察時に存在していて、臨床的状态と何らかの関連性をもつ可能性のある治癒した変化に向けられた。

臨床的な検討は、2年ごとに実施された検診結果の記録に基づいて剖検所見や放射線被曝状態を伏せて行った。ある場合には終末疾患の病歴も入手することができた。心臓疾患、高血圧および糖尿病の形跡の有無について臨床記録の検討を実施した。入手し得る心電図はいずれも再検討し、ABCCの臨床的コード<sup>19</sup>およびWHOのコード<sup>20</sup>に従って符号化した。心電図検査における心筋硬塞の形跡としては、符号化し得るQRS異常、心内膜下硬塞を示唆するST-T変化および時期別の記録における経時的変化などがある。ABCCの臨床的コードの分類基準に従って診断確実あるいは診断不確実と符号化した。<sup>19</sup> 診断確実および診断不確実の高血圧、高血圧性心臓疾患および糖尿病の判定基準は、付録Aに記述する。

剖検実施の承諾は、臨床診断を知っていない剖検連絡員によって求められた。すべての剖検診断を再検討し、主要死因を符号化した。三つの主要な冠状動脈の近位部5cmにおけるアテローム性動脈硬化症の程度の評定は米国心臓協会の写真パネル法に従った。ただし、血管全体についての評価値は、変化の範囲や程度とは関係なく、管腔の狭窄または閉塞を示す部位に基づいて決定するという修正を加えた。<sup>21-23</sup> 記録されたアテローム性動脈硬化症の最高評価値とその他の観察結果との相関関係を調べた。

各例について心臓から少なくとも7枚の組織切片を取った。最初の4枚は、大体において心室の中部3分の1と上部3分の1の境界付近から心臓基底部に平行して切出し、次の部位を含めるようにした。すなわち、1)心室の中隔の前部およびそれに隣接する両心室前部、2)前乳頭筋を

3) posterolateral left ventricle including the posterior papillary muscle, and 4) lateral right ventricle. Sections 5 and 6 were taken perpendicular to the previous sections. Section 5 contained the posterior leaf of the mitral valve and the posterior left ventricle. Section 6 included the noncoronary aortic cusp, the AV node and bundle of His, and intraventricular septum. Section 7 was taken from the cardiac apex. Histologic sections were routinely stained with hematoxylin and eosin. In addition Masson trichrome, Weigert-van Gieson elastic, basic fuchsin picric acid, PAS, alcian blue, and Gomori aldehyde fuchsin-Masson trichrome stains, and stains for reticulum, iron, lipofuscin, and amyloid were used when indicated. The slides were examined without knowledge of the clinical findings, the gross autopsy observations, the final autopsy diagnosis, or the estimated radiation dose.<sup>24</sup> Papillary muscle was not present in the sections from two autopsies. Consequently, papillary muscle fibrosis and small vessel sclerosis of papillary muscle were recorded for 373 cases and intramural small vessel sclerosis was recorded for 375 cases in the tables and analyses.

The following definitions applied to lesions observed in histologic sections. Healed myocardial infarcts were scarred areas measuring at least 0.5 cm in one dimension. Small foci of myocardial fibrosis involved areas of ventricular wall less than 0.5 cm in diameter but with definite replacement of muscle fibers by scar tissue. Areas of interstitial or perivascular fibrosis were not included. Papillary muscle fibrosis (PMF), diffuse type, consisted of non-demarcated fibrosis which frequently extended to the endothelial surface of the papillary muscle (Figure 1). PMF focal type did not extend to the endothelial surface but was separated from the endocardium by a rim of palisade of viable muscle fibers (Figure 2). Areas of both diffuse and focal PMF were present in some histologic sections. Small vessel sclerosis (SVS) applied to mural and papillary small arteries. The sclerosed vessel wall was often hyalinized, showed alteration of elastic and muscle layers, and was frequently accompanied by marked proliferation of perivascular tissue (Figure 3). The types of vascular sclerosis and alterations in the epicardial vessels were not recorded but the presence of SVS (papillary) of each papillary muscle and of SVS (mural) was recorded separately.

## RESULTS

Of the subjects in the autopsy sample, 54% were women and 52% were aged 70 or more at the time of death (Table 1). There was no age or sex difference in the prevalence of SVS (papillary and mural) or

含む左心室前外側部, 3) 後乳頭筋を含む左心室後外側部および 4) 右心室外側部. 第5および第6枚目の切片は, 前述の切片に対して垂直に切出した. 切片5は僧帽弁後尖と左心室後部を含む. 切片6には大動脈弁非冠動脈尖, 房室結節と His 束並びに心室間中隔が含まれていた. 切片7は, 心尖部から取った. 組織切片には通常ヘマトキシリン・エオジン染色した. そのほか, 必要に応じて Masson trichrome, Weigert-van Gieson elastic, basic fuchsin picric acid, PAS, alcian blue および Gomori aldehyde fuchsin-Masson trichrome 染色ならびに細網線維, 鉄, リポフスチンおよびアミロイド染色法を使用した. 標本の鏡検に当たって臨床所見, 肉眼的剖検所見, 最終的剖検診断や推定放射線量<sup>24</sup>などが分からないようにしておいた. 剖検2例から得た切片では, 乳頭筋が含まれていなかった. したがって, 集計表および解析では, 乳頭筋線維症および乳頭筋における小血管硬化症は373例について記録されており, 心壁内小血管硬化症は375例について記録された.

組織切片に観察された病変に対しては, 次の定義を適用した. 治癒した心筋硬塞とは, 一方向の直径が少なくとも0.5 cmの癒痕形成部である. 心筋線維症の小病巣とは, 直径0.5 cm以下の心室壁の変化で, 癒痕組織による筋線維の明確な置換を示すものである. なお, 今回の検討に間質性または血管周囲の線維症は含めなかった. 乳頭筋線維症 (PMF) の瀰漫型とは, 境界の不鮮明な線維症であり, 乳頭筋の内皮表面まで及ぶことがしばしばあった (図1). 限局型乳頭筋線維症とは, 辺縁に残存する筋線維の壁によって心内膜から隔てられていて内皮表面まで及ぶことのないものである (図2). 瀰漫型および限局型乳頭筋線維症の併発を示す部分が若干の組織切片にみられた. 小血管硬化症 (SVS) は, 心壁内および乳頭筋の小動脈について記録した. 硬化した血管壁は硝子化を呈することがしばしばであり, 内弾性板および筋層の変化を示し, また, 血管周囲の組織の著しい増殖を伴うことが多い (図3). 血管硬化症および心外膜血管の変化の種類は記録しなかったが, 各乳頭筋におけるSVS (乳頭筋) の存在およびSVS (心壁内) の存在をそれぞれ別に記録した.

## 結 果

剖検例の中で今回の調査の対象となったものの54%は女性で, 52%は死亡時に70歳以上であった (表1). SVS (乳頭筋および心壁内) またはPMF (瀰漫型) の有病率に

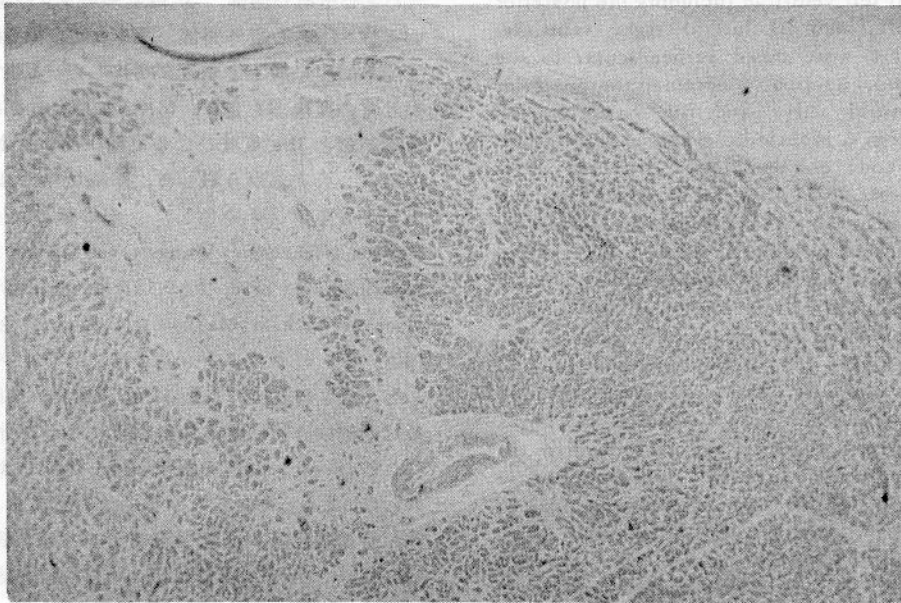


Figure 1 Papillary muscle fibrosis, diffuse type. Sclerosed vessel at apex with fibrosis extending to the endocardial surface. H&E  $\times 10$

図1 瀰漫型乳頭筋線維症。先端部に硬化を示す血管があり、線維症は心内膜表面まで及んでいる。ヘマトキシリン・エオジン染色、 $\times 10$

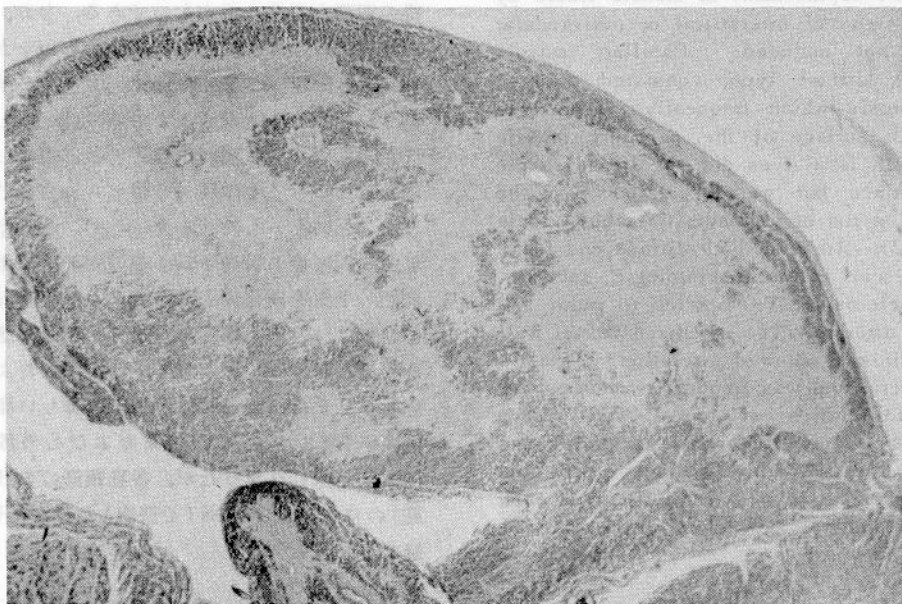


Figure 2 Papillary muscle fibrosis, focal type. Sharply demarcated fibrosis with viable subendocardial and perivascular palisades of muscle. H&E  $\times 10$

図2 限局型乳頭筋線維症。心内膜下および血管周囲に壁状の筋層の残存を示す境界の鮮明な線維症。ヘマトキシリン・エオジン染色、 $\times 10$

TABLE 1. PERCENTAGE OF AUTOPHYG WITH CAPILLARY SMALL VESSEL SCLEROSIS AND PAVILLARY MUSCLE FIBROSIS BY SEX AND AGE

Age (yr)	Sex	Autophagy (%)	Capillary small vessel sclerosis (%)	Papillary muscle fibrosis (%)
20-29	Male	10	5	2
30-39	Male	15	10	5
40-49	Male	20	15	10
50-59	Male	25	20	15
60-69	Male	30	25	20
70-79	Male	35	30	25
80-89	Male	40	35	30
90-99	Male	45	40	35
20-29	Female	10	5	2
30-39	Female	15	10	5
40-49	Female	20	15	10
50-59	Female	25	20	15
60-69	Female	30	25	20
70-79	Female	35	30	25
80-89	Female	40	35	30
90-99	Female	45	40	35

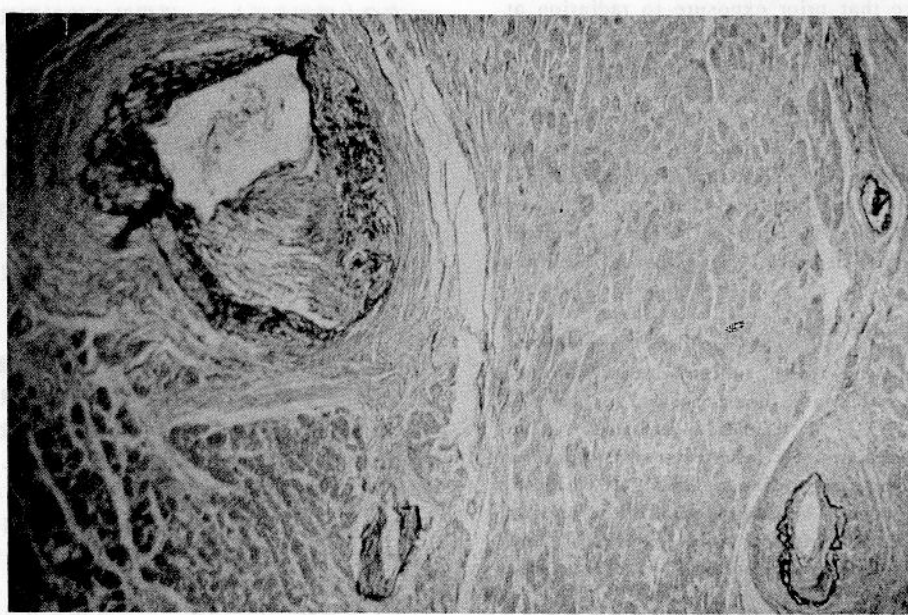
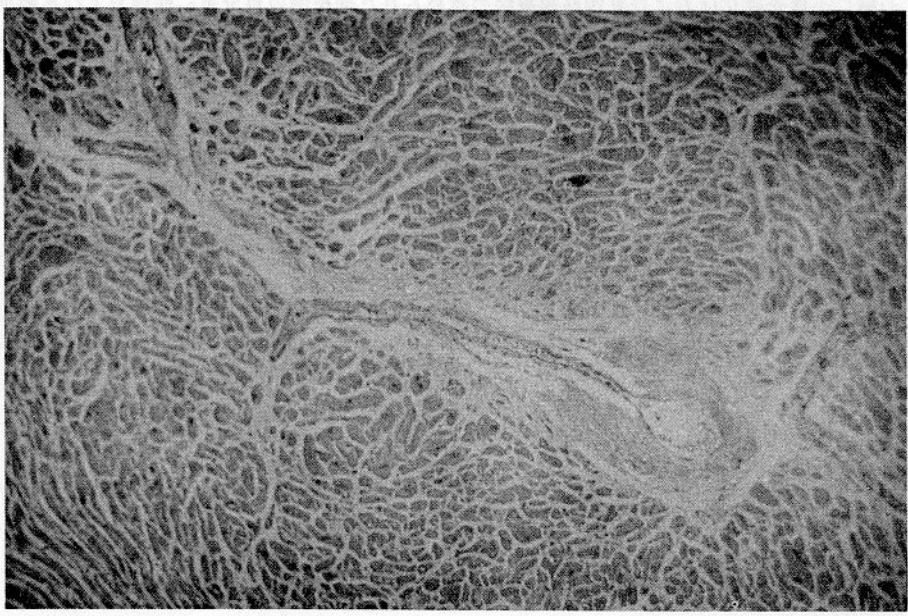


Figure 3 Small vessel sclerosis in papillary muscle. Elastic stain  $\times 40$

図3 乳頭筋における小血管硬化症. 弾力線維染色,  $\times 40$

TABLE 1 PERCENTAGE OF AUTOPSIES WITH CARDIAC SMALL VESSEL SCLEROSIS AND PAPILLARY MUSCLE FIBROSIS BY SEX AND AGE

表1 心臓に小血管硬化症および乳頭筋線維症の認められた剖検例の百分率：性別および年齢別

	Autopsies	Small Vessel Sclerosis		Papillary Muscle Fibrosis		
		Mural	Papillary	Diffuse	Diffuse/Focal	Focal
Total	373	(267)	(325)	(169)	(34)	(16)
Male	171	69.9%†	87.1%	45.0%	9.4%	5.8%
Female	202	72.3	87.1	45.5	8.9	3.0
Test		NS	NS	NS	NS	NS
Age at Death						
≤ 49	28	50.0	75.0	42.9	—	3.6
50-59	34	73.5	94.1	38.2	2.9	—
60-69	117	70.9	84.6	45.3	6.0	1.7
70-79	125	71.2	89.6	47.2	12.0	6.4
80+	69	78.9‡	88.4	46.4	15.9	7.2
Linear trend with age		NS	NS	NS	*	*

Parentheses indicate the number of autopsies in each category

† Based on 173 males

‡ Based on 71 subjects

\* 0.01 < P < 0.05

PMF (diffuse). However, PMF (diffuse and focal) and PMF (focal) increased significantly with age. There was no evidence that prior exposure to radiation at the time of the bomb was related to the presence of vessel sclerosis or muscle fibrosis (Table 2).

PMF (focal) was significantly related ( $P < 0.01$ ) to cardiovascular disease as a cause of death, to coronary artery atherosclerosis, to healed myocardial infarction in histologic sections, and to increased heart weight (Table 3) but not to hypertension, hypertensive heart disease, or diabetes mellitus (Table 4).

Both PMF (diffuse) and SVS (papillary) showed no relation to coronary artery atherosclerosis score, hypertensive heart disease, heart weight, myocardial infarction (by ECG), or diabetes mellitus. SVS (papillary) was significantly less frequent in persons who died of cardiovascular disease, and PMF (diffuse) was less frequent when healed myocardial infarction was present. SVS (mural and papillary) and PMF (diffuse) were more frequent in subjects who had hypertension.

At all ages there was more small vessel sclerosis of the anterior than of the posterior papillary muscle when only one muscle was involved (Table 5). SVS in only one papillary muscle tended to decrease in frequency, and vessel sclerosis in both muscles to increase in frequency with advancing age.

は年齢差も男女差もなかった。しかしながら、PMF (瀾漫型および限局型) および PMF (限局型) は年齢とともに有意な増加を示した。原爆時の放射線被曝が血管硬化症または筋線維症の有無に関係があるとの証拠は認められなかった (表 2)。

PMF (限局型) は、死因としての心臓血管疾患と有意な関係 ( $P < 0.01$ ) があり、組織切片における冠状動脈のアテローム性硬化症および治癒した心筋硬塞とも、また、心臓重量の増加とも有意な関係があった (表 3)。しかし、高血圧、高血圧性心臓疾患または糖尿病とは関係なかった (表 4)。

PMF (瀾漫型) も SVS (乳頭筋) も冠状動脈のアテローム性硬化症評価値、高血圧性心臓疾患、心臓重量、心筋硬塞 (心電図所見) または糖尿病と全く関係なかった。SVS (乳頭筋) の頻度は、心臓血管疾患で死亡した者に有意に少なく、PMF (瀾漫型) は、治癒した心筋硬塞のある者に少なかった。SVS (心壁内および乳頭筋) および PMF (瀾漫型) は、高血圧のあった者に高い頻度で認められた。

いずれの年齢においても、一つの筋肉だけに小血管硬化症があった場合、それは後乳頭筋よりも前乳頭筋において認められることが多かった (表 5)。年齢が高くなるにつれて、一つの乳頭筋だけに SVS が認められる例の頻度が減少し、両乳頭筋に血管硬化症が存在する頻度の増大する傾向があった。

TABLE 2 PERCENTAGE OF AUTOPSIES WITH CARDIAC SMALL VESSEL SCLEROSIS AND PAPILLARY MUSCLE FIBROSIS BY ESTIMATED RADIATION DOSE AT THE TIME OF THE BOMB

表2 心臓に小血管硬化症および乳頭筋線維症の認められた剖検例の百分率：原爆時の推定放射線量別

T65 Dose in Rad	Autopsies	Small Vessel Sclerosis		Papillary Muscle Fibrosis		
		Mural	Papillary	Diffuse	Diffuse/Focal	Focal
Total	373	(267)	(325)	(169)	(34)	(16)
0.9+ NIC	195	68.9%†	87.7%	44.6%	7.2%	4.1%
10-99	101	74.5 ‡	84.2	44.6	9.9	5.0
100+	77	72.7	89.6	48.1	13.0	3.9
Radiation effect (100+ vs 0.9+ NIC)		NS	NS	NS	NS	NS

Parentheses indicate the number of autopsies in each category.

† Based on 196 subjects

‡ Based on 102 subjects

NIC — Not in city ATB

TABLE 3 PERCENTAGE OF AUTOPSIES WITH SMALL VESSEL SCLEROSIS AND PAPILLARY MUSCLE FIBROSIS BY AUTOPSY CAUSE OF DEATH, HEART WEIGHT, HIGHEST CORONARY ATHEROSCLEROSIS SCORE, AND MYOCARDIAL INFARCTION AT AUTOPSY

表3 小血管硬化症および乳頭筋線維症の認められた剖検例の百分率：剖検死因別、心臓重量別、冠状動脈アテローム性硬化症の最高評価点別および剖検における心筋硬塞の有無別

	Autopsies	Small Vessel Sclerosis		Papillary Muscle Fibrosis		
		Mural†	Papillary	Diffuse	Diffuse/Focal	Focal
Cause of death	373	(267)	(325)	(169)	(34)	(16)
Cardiovascular Disease	27	71.4%	70.4%	37.0%	33.3%	18.5%
Cerebrovascular disease	86	73.6	91.9	48.8	9.3	1.2
Cancer	112	67.0	87.5	50.0	3.6	2.7
Remainder	148	73.0	87.2	41.2	8.8	4.7
Test: Cardiovascular disease vs all others		NS	*	NS	**	**
Highest coronary score	373					
1-2	209	69.0	86.6	45.9	4.8	1.9
3-4	117	72.0	88.0	46.2	7.7	4.3
5-6	47	78.7	87.2	40.4	31.9	14.9
Linear trend with coronary score		NS	NS	NS	**	**
Healed myocardial infarct at autopsy	373					
Absent	301	69.1	88.0	45.5	1.7	0.7
Present	72	79.7	83.3	27.8	40.3	19.4
Test: Present vs Absent		NS	NS	**	**	**
Heart weight ‡	369	(263)	(321)	(167)	(34)	(15)
< 249 gm	113	77.0	88.5	39.8	8.0	1.8
250-299	89	68.9	89.9	50.6	4.5	3.4
300-349	72	63.9	90.3	52.8	8.3	1.4
350+	95	70.8	80.0	41.1	15.8	9.5
Linear trend with heart weight		NS	NS	NS	*	*

Parentheses indicate the number of autopsies in each category.

† Based on two additional autopsies in which papillary muscles were unavailable.

\* 0.01 < P < 0.05; \*\* P < 0.01

‡ Heart weight unavailable in 4 cases.

TABLE 4 PERCENTAGE OF AUTOPSIES WITH SMALL VESSEL SCLEROSIS AND PAPILLARY MUSCLE FIBROSIS BY CLINICAL DIAGNOSIS OF HYPERTENSION, HYPERTENSIVE HEART DISEASE, MYOCARDIAL INFARCTION BY ELECTROCARDIOGRAM, AND DIABETES MELLITUS

表4 小血管硬化症および乳頭筋線維症の認められた剖検例の百分率：高血圧，高血圧性心臓疾患，心電図による心筋硬塞および糖尿病の臨床診断の有無別

	Autopsies †	Small Vessel Sclerosis		Papillary Muscle Fibrosis		
		Mural†	Papillary	Diffuse	Diffuse/Focal	Focal
Hypertension	370	(264)	(323)	(168)	(34)	(15)
None	106	60.4	80.2	36.8	3.8	0.9
Possible	170	73.1	91.8	50.0	10.0	5.9
Definite	94	78.9	87.2	46.8	13.8	4.3
Test		**	*	*	*	NS
Hypertensive heart disease	244	(184)	(221)	(118)	(30)	(14)
None (but hypertensive)	51	66.6	90.2	41.2	7.8	3.9
Possible	143	75.1	91.6	50.3	11.9	6.3
Definite	50	82.0	88.0	50.0	18.0	6.0
Test		NS	NS	NS	NS	NS
Myocardial infarction (ECG)	342	(240)	(298)	(151)	(34)	(15)
None	265	68.1	85.3	43.8	6.4	3.8
Possible	63	73.5	93.7	50.8	14.3	4.8
Definite	14	85.7	92.9	21.4	57.1	14.3
Test		NS	NS	NS	**	NS
Diabetes mellitus	367	(261)	(320)	(166)	(34)	(15)
None	278	72.1	87.4	43.5	8.6	3.2
Possible	56	63.2	85.7	48.2	7.1	7.1
Definite	33	72.8	87.9	54.5	18.2	6.1
Test		NS	NS	NS	NS	NS

Parentheses indicate the number of autopsies in each category.

† Based on two additional autopsies in which papillary muscles were unavailable.

† Cases in which clinical data were insufficient to assign a diagnosis were omitted from the corresponding tables. Cases who were normotensive were also omitted from the table for Hypertensive Heart Disease.

\*  $0.01 < P < 0.05$ ; \*\*  $P < 0.01$ ; Test — possible and definite vs none.

TABLE 5 PERCENTAGE OF AUTOPSIES WITH PAPILLARY MUSCLE SMALL VESSEL SCLEROSIS BY AGE AT DEATH

表5 乳頭筋に小血管硬化症の認められた剖検例の百分率：死亡時年齢別

Age at Death	Autopsies	Small Vessel Sclerosis		
		Papillary Muscle		
		Ant.	Post.	Ant. & Post.
≤ 49	28	28.6%	21.4%	25.0%
50-59	34	35.3	26.5	32.4
60-69	117	29.9	10.3	44.4
70-79	125	26.4	13.6	49.6
80+	69	23.2	17.4	47.8
Total	373	27.9	15.0	44.2
Linear trend with age		NS	NS	*

\*  $0.01 < P < 0.05$

SVS (papillary) was more frequent when PMF (diffuse) was present and less frequent when PMF (focal) was present. SVS (mural) was observed more often when PMF (focal) was present but the association was not statistically significant (Table 6). The association between SVS (papillary) and PMF (diffuse) was further demonstrated when each muscle was examined separately (Table 7). SVS was particularly frequent when diffuse fibrosis was present in the same papillary muscle. In approximately 70% of the cases in which the diffuse type of fibrosis occurred in both papillary muscles, each muscle also contained sclerosed vessels.

SVS (乳頭筋)の頻度は、PMF (瀰漫型)がある場合に高く、PMF (限局型)がある場合に低かった。SVS (心壁内)は、PMF (限局型)がある場合に多かったが、その関連性は統計的には有意でなかった(表6)。各筋肉を別々にみると、SVS (乳頭筋)とPMF (瀰漫型)との関連性は、一層明確に認められる(表7)。瀰漫型線維症が存在する場合、その同一乳頭筋においてSVSが特に多かった。両乳頭筋に瀰漫型線維症の発生が認められた症例の約70%において、両筋肉に血管の硬化症もみられた。

TABLE 6 PERCENTAGE OF AUTOPSIES WITH SMALL VESSEL SCLEROSIS OF PAPILLARY MUSCLES (BY LOCATION) AND OF MURAL MYOCARDIUM BY TYPE OF PAPILLARY MUSCLE FIBROSIS

表6 乳頭筋に小血管硬化症(部位別)および心壁内に心筋小血管硬化症の認められた剖検例の百分率: 乳頭筋線維症の種類別

Papillary Muscle Fibrosis	Autopsies	Small Vessel Sclerosis				
		Papillary Muscle				Mural
		Ant.	Post.	Ant. & Post.	Total	
Diffuse	169	25.4%	13.0%	57.4%	95.8%	75.7%
Diffuse and focal	34	32.4	14.7	47.1	94.2	79.4
Focal	16	18.8	6.3	31.3	56.4	87.5
None	154	30.5	18.2	30.5	79.2	62.3
Total	373	27.9	15.0	44.2	87.1	71.0
Test: Diffuse vs none		NS	NS	**	**	*
Diffuse and focal vs none		NS	NS	NS	NS	NS
Focal vs none		NS	NS	NS	NS	NS

\* 0.01 < P < 0.05; \*\* P < 0.01

TABLE 7 PERCENTAGE OF AUTOPSIES WITH PAPILLARY SMALL VESSEL SCLEROSIS (BY LOCATION) AND TYPE OF PAPILLARY MUSCLE FIBROSIS

表7 乳頭筋に小血管硬化症(部位別)の認められた剖検例の百分率および乳頭筋線維症の種類

Papillary Fibrosis		Autopsies	Papillary Muscle Small Vessel Sclerosis		
Muscle	Type		Anterior	Posterior	Ant. & Post.
Anterior	Diffuse	62	50.0%	3.2%	45.2%
Posterior	Diffuse	48	8.3	27.1	56.3
Anterior	Focal or D/F	8	37.5	-	37.5
Posterior	Focal or D/F	5	-	40.0	20.0
Ant. & Post.	Diffuse	59	13.6	11.9	71.2
Ant. & Post.	Focal and/or D/F	15	26.7	-	46.7
Anterior	Diffuse	13	46.2	7.7	46.2
Posterior	Focal or D/F				
Anterior	Focal or D/F	9	11.1	33.3	44.4
Posterior	Diffuse				
No fibrosis		154	30.5	18.2	30.5
Total		373	27.9	15.0	44.2



## DISCUSSION

PMF (diffuse) is unequivocally different from PMF (focal) in histological character and pathogenesis. The diffuse type is related to and apparently a result of the sclerosis of the small vessels of the papillary muscles, with attendant chronic progressive local ischemia. The fibrosis extends to the endothelial surface without reactive endothelial proliferation and without sparing of subendothelial muscle fibers. PMF (diffuse) is not related to coronary heart disease in the usual sense of large vessel atherosclerosis and in this series of autopsies is not related to myocardial infarction, cardiac hypertrophy, hypertensive heart disease, and diabetes mellitus. It is more prevalent however in those with hypertension. It is found in almost half of the autopsies and evidently produces no recognizable clinical signs or symptoms.

SVS (papillary) also appears to be an independent process related and probably antecedent to PMF (diffuse) but unrelated to coronary heart disease, myocardial infarction, cardiac hypertrophy, diabetes mellitus, or other recognizable clinical processes with the possible exception of hypertension. Not infrequently, SVS (papillary) is seen in an otherwise normal papillary muscle but the reverse, PMF (diffuse) without SVS (papillary), is less frequent. The distribution of the sclerosed small vessels in histologic sections and their proximity and anatomical relation to areas of PMF (diffuse) (Figure 4) also indicate the direct relation between the vascular and fibrotic changes.

SVS (papillary) may develop earlier in one papillary muscle than in the other so that involvement of both muscles is more frequent in older persons. The sclerotic change evidently progresses very slowly. There is no evidence that a bypass circulation is established although not infrequently the sclerosis appears to be focal and nodular in vessels sectioned longitudinally (Figure 4). This association of SVS (papillary) and PMF (diffuse) results in a chronic progressive change. Acute necrosis, cellular infiltration, fibroblastic activity, and revascularization are not observed. This is in sharp contrast to PMF (focal), the development of which can be traced through all stages of infarction from acute necrosis to the healed scar.

SVS (mural) is less frequent than SVS (papillary). An anatomical relation between SVS (mural) and areas of fibrosis in the wall of the ventricle is usually not evident. Analysis of the data suggests that there is a relation between sclerosis of these vessels and hypertension, but not with diabetes. Although there was a gradient of the prevalence

## 考 察

PMF (瀰漫型)の組織学的特徴および病理発生はPMF (限局型)と異なることは確かである。この瀰漫型は、慢性進行性局所的虚血を伴う乳頭筋の小血管硬化症に関係があり、かつ、その結果生じたものであると思われる。この種の線維症は、反応性内皮増殖を伴うことなく、また、内皮下筋線維が置換を免れることもないので上皮表面までに及ぶ。PMF (瀰漫型)は、大血管におけるアテローム性動脈硬化症という通常の場合のように冠状動脈性心臓疾患との関係はなく、また、今回の剖検例では、心筋硬塞、心臓肥大、高血圧性心臓疾患および糖尿病との関係もなかった。しかしながら、高血圧のある者にPMF (瀰漫型)の有病率が高いことが認められた。PMF (瀰漫型)は、剖検例のほとんど半数に認められ、認識できるような臨床的徴候または症状を発現することはないようである。

SVS (乳頭筋)も独立した疾病過程であり、PMF (瀰漫型)と関係があり、恐らくPMF (瀰漫型)に先行するものと思われるが、冠状動脈性心臓疾患、心筋硬塞、心臓肥大、糖尿病またはその他の認識し得る臨床的な過程とは無関係である。ただし、恐らく高血圧は例外と思われる。別に異常のない乳頭筋にSVS (乳頭筋)が認められることはまれではないが、逆にSVS (乳頭筋)を伴わないPMF (瀰漫型)はまれである。組織切片におけるSVSの分布およびそれとPMF (瀰漫型)の部位との位置的關係や解剖学的的關係(図4)も血管の変化および線維症性変化との間に直接的な關係のあることを示す。

SVS (乳頭筋)は、いずれか一方の乳頭筋により早く発現することもあるので、両乳頭筋に変化が認められる頻度は高年齢ほど高くなる。硬化性変化の進展は極めて遅いようである。血管を縦に切開してみると、硬化症が限局性で結節状であることはまれではないが、副側循環ができるという証拠はない(図4)。SVS (乳頭筋)とPMF (瀰漫型)とのこのような併発の結果、慢性的な進行性の変化が生じる。急性壊死、細胞浸潤、線維芽細胞活動および脈管再生はみられない。これは、PMF (限局型)と対照的であり、後者の場合は、急性壊死から治癒した瘢痕に至るまでの硬塞のすべての段階にわたってその展開を追跡することができる。

SVS (心壁内)は、SVS (乳頭筋)よりも低頻度である。SVS (心壁内)と心室壁における線維症の部位との解剖学的關係は、通例明白ではない、資料の解析の結果では、これらの血管の硬化症と高血圧との間には關係があるが、糖尿病とは關係がないことが示唆された。冠状動脈性心臓疾患および高血圧性心臓疾患においてSVS (心壁内)

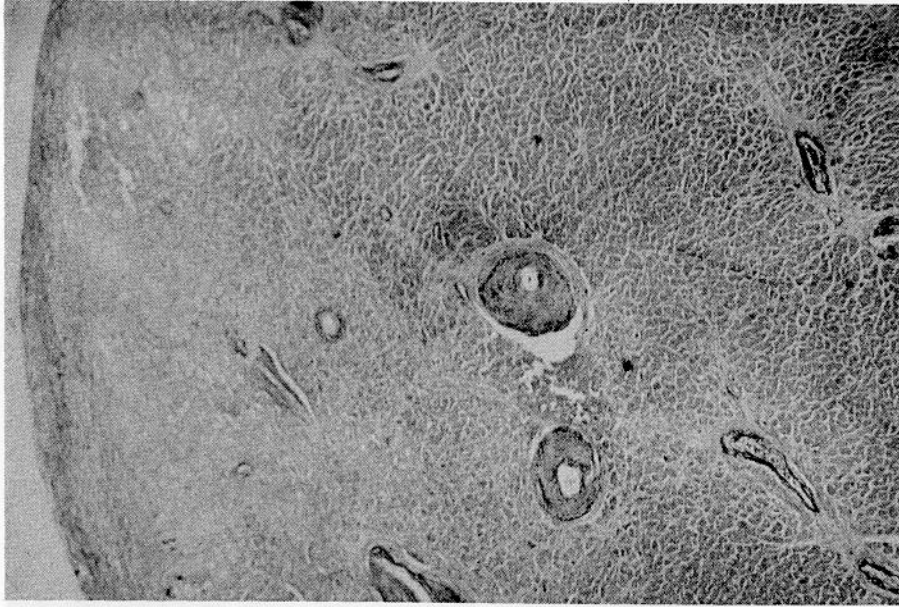


Figure 4 Small vessel sclerosis in papillary muscle and relation to area of diffuse type of papillary muscle fibrosis. Gomori aldehyde fuchsin-Masson trichrome  $\times 10$

図4 乳頭筋における小血管硬化症および瀰漫型乳頭筋線維症の部位との関係。Gomori aldehyde fuchsin - Masson trichrome 染色,  $\times 10$

of SVS (mural) with coronary heart disease and with hypertensive heart disease, these gradients were not statistically significant.

A narrow and sharply demarcated rim of surviving muscle fibers is usually present between the endocardium and an underlying myocardial infarct, and similar fibers may persist about thebesian veins.<sup>25</sup> This has been long recognized and is commonly described in textbooks. It has been suggested that the muscle fibers survive because of the direct transfer of oxygen and other vital nutrients through the endocardium from the blood in the ventricular chamber. There is little variation in the width of this layer of surviving muscle which has been said to be equal to the width of the non-vascularized subendothelial layer of large vessels. PMF (focal) characteristically and consistently demonstrates a similar layer of surviving and morphologically normal muscle fibers which appear like a regular and even palisade beneath the endocardium. Several facts challenge the theory that these palisades of muscle fibers owe their survival to endocardial transfer of nutrients during ischemic episodes. In both myocardial infarction and PMF (focal), subendocardial fibers survive even when there is marked thickening and elastosis of the endocardium which should obstruct the transfer of oxygen (Figure 5). These subendocardial muscle fibers do not survive in PMF (diffuse) which is an

の頻度の増加傾向がみられたが、これらは統計学的に有意ではなかった。

心内膜とその下層の心筋硬塞との間に残存筋線維の境界鮮明な薄い層が介在することが多く、同じような筋線維が最小心臓静脈の周囲にも残存する場合がある。<sup>25</sup> このことは以前から知られていたことであり、一般に教科書にも記載されている。心室内の血液から酸素やその他の重要な栄養が心内膜を透過して直接供給されるために、筋線維が残存するのであろうと示唆されている。この残存筋層の幅はほとんど一定であり、大血管の内皮下における血管形成のない層の幅に等しいといわれている。PMF (限局型)では、一貫して同様の形態学的に正常な残存筋線維層がみられることが特徴であり、それは心内膜下に規則正しい均一な壁として認められる。虚血性疾患の際に心内膜を経て栄養の供給を受けるためにこの種の壁状の筋線維層が残存するという説に対してはいくつかの反証がある。心筋硬塞およびPMF (限局型)のいずれにおいても、酸素の供給の障害となるような心内膜の著しい肥厚や弾力線維症がある場合にさえも心内膜下に筋線維の残存が認められる(図5)。局所的な小血管疾患

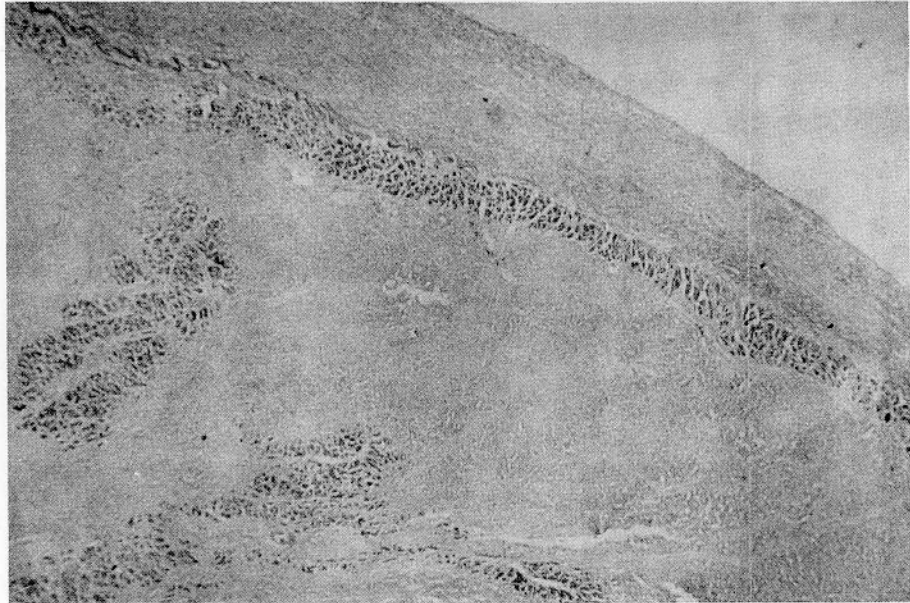


Figure 5 Endocardial fibroelastosis and focal type papillary muscle fibrosis with viable subendocardial and perivascular palisades of muscle. H&E  $\times 10$

図5 心内膜下および血管周囲に壁状の筋層の残存を伴う心内膜弾力線維症および局限型乳頭筋線維症。ヘマトキシリン・エオジン染色， $\times 10$

ischemic result of local small vessel disease, even though in this type of fibrosis there is no observable endocardial change. Palisades of viable muscle fibers are also found about infarcts deep within the myocardium and away from the endocardial or epicardial surfaces. These surviving muscle fibers are located at the periphery of muscle bundles where thin-walled vessels are found. It has been established that there is normally a rich anastomosis of small vessels beneath the endocardium, and it is more likely that the muscle fibers at the periphery of myocardial infarcts and PMF (focal) survive because they are supplied by these vessels.

These observations provide additional evidence against the theory that ischemic heart disease results from simple mechanical obstruction of blood flow. In most cases coronary artery atherosclerosis and obstruction is an essential feature in the development of myocardial infarction but it is not always a sufficient explanation. The absence of small vessel disease, the distribution of lesions at a distance from the area of vascular obstruction, and the sharp demarcation of the surviving peripheral muscle fibers all suggest that in addition to the essential ischemia, there are local differences in the myocardium which make some areas more susceptible to circulatory deficit than others.<sup>26</sup>

のための虚血の結果であるPMF(瀰漫型)では、心内膜の変化がないにもかかわらず、この種の心内膜下筋線維層の残在はない。心内膜または心外膜表面から離れた心筋内の深部における硬塞の周囲にも壁状の筋線維層が見いだされる。これらの残存筋線維は、壁の薄い血管の認められる筋束周囲部に位置している。心内膜下には普通豊富な小血管吻合があることが証明されているので、心筋硬塞およびPMF(局限型)の周囲部における筋線維は、これらの血管によって血液が供給されるために残存する可能性がもっと強い。

以上の観察結果は、虚血性心疾患が血流の単純な機械的障害に起因するという説に対する一層の反証となるものであろう。冠状動脈のアテローム性動脈硬化症および閉鎖は、心筋硬塞症の発現における重要な特色であることが多いが、それだけでは十分な説明ができない場合もある。小血管疾患が欠如していること、血管閉鎖部から離れたところに病変が分布していることおよび周辺部における残存筋線維層の境界が鮮明であることは、本態性虚血の問題以外に、心筋層には局所的な差異があり、ある部位は他の部位よりも循環障害を受けやすいことを示唆する。<sup>26</sup>

## APPENDIX A CRITERIA FOR CLINICAL EVALUATIONS

### 付 録 臨 床 的 判 定 基 準

#### Hypertension

**Definite.** Blood pressure of 160mmHg or higher systolic and 95mmHg or higher diastolic on two or more examinations.

**Possible.** Blood pressure 140mmHg or higher systolic or 90mmHg or higher diastolic on two or more examinations, when not classifiable as definite.

#### Hypertensive Heart Disease

**Definite.** Definite hypertension (see above) plus any of the following: moderate cardiomegaly (X-ray), atrial fibrillation, left bundle branch block, left axis deviation, or ST depression or T wave inversion of 1.0mm or more.

**Possible.** Definite or possible hypertension (see above) plus any of the following: mild cardiomegaly (X-ray), premature beats, atrial fibrillation, nodal rhythm, AV or intraventricular block, P wave abnormalities, left axis deviation, high voltage of QRS, left ventricular hypertrophy or strain, or ST depression or T wave abnormalities, when not codable as definite.

#### Diabetes Mellitus

**Definite.** Serum glucose values exceeding any of the following on two or more examinations: Fasting 125mg/100ml; 1-hour 215mg/100ml; 2-hour 145mg/100ml; or 3-hour 130mg/100ml.

**Possible.** Urine or serum glucose values equal or exceeding any of the following on one or more examinations: urine glucose 1+; fasting 105mg/100ml; 1-hour 175mg/100ml; 2-hour 140mg/100ml; or 3-hour 120mg/100ml. Glycosuria with concomitant serum glucose values in the normal range was not considered evidence of diabetes mellitus.

#### 高血圧

診断確定. 2回以上の診察において収縮期血圧が160mmHg以上および拡張期血圧が95mmHg以上.

診断不確定. 診断確定として分類されないもので, 2回以上の診察において収縮期血圧が140mmHg以上, または, 拡張期血圧が90mmHg以上.

#### 高血圧性心臓疾患

診断確定. 診断確定な高血圧(上記参照)に加えて次のいずれかを有するもの: 中等度の心臓肥大(X線検査所見), 心房細動, 左脚ブロック, 左軸偏位, またはST低下あるいは1.0mm以上のT波陰性化.

診断不確定. 診断確定または不確定な高血圧(上記参照)に加えて次のいずれかを有するもの: 軽度の心臓肥大(X線検査所見), 期外収縮, 心房細動, 結節性調律, 房室または心室内ブロック, P波異常, 左軸偏位, QRS高電位差, 左心室肥大または緊張像, あるいはST低下またはT波異常があつて, 診断確定として符号化できないもの.

#### 糖尿病

診断確定. 2回以上の検査において血清糖値が次の値のいずれかを越えるもの: 空腹時125mg/100ml; 1時間値215mg/100ml; 2時間値145mg/100ml; または3時間値130mg/100ml.

診断不確定. 1回以上の検査において尿糖値または血清糖値が次の値のいずれかに等しいか, またはそれ以上であるもの: 尿糖+; 空腹時105mg/100ml; 1時間値175mg/100ml; 2時間値140mg/100ml; または3時間値120mg/100ml. 糖尿が正常範囲の血清糖値を付随していた場合は糖尿病の徴候と考えなかった.

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