ISCHEMIC HEART DISEASE IN PATIENTS WITH BUNDLE-BRANCH BLOCK

Peter Eriksson

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ISCHEMIC HEART DISEASE IN PATIENTS WITH BUNDLE-BRANCH BLOCK

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I **Eriksson P, Hansson P-O, Eriksson H, Dellborg M.** Bundle-branch block in a general male population. The Study of Men Born 1913. *Circulation 1998, in press.*

II **Eriksson P, Andersen K, Swedberg K, Dellborg M.** Vectorcardiographic monitoring of patients with acute myocardial infarction and chronic bundle branch block. *European Heart Journal* 1997;18:1288-1295.

III **Eriksson P, Gunnarsson G, Dellborg M.** Diagnosis of acute myocardial infarction in patients with chronic right bundle-branch block using standard 12-lead electrocardiogram compared with dynamic vectorcardiography. *Cardiology* 1998;90:58-62.

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V **Eriksson P, Albertsson P, Ekström L, Dellborg M.** Continuous vectorcardiographic monitoring of ischemia during coronary angioplasty in patients with bundle-branch block. *Submitted for publication.*

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Peter Eriksson, Clinical Experimental Research Laboratory, Department of Medicine, Sahlgrenska University Hospital/Östra, Institute of Heart and Lung Diseases, Göteborg University, Göteborg, Sweden.

Abstract

We have studied a random sampled population of 855 men aged 50, who were monitored from 1963 to 1993. The prevalence of bundle-branch block increased from 1% at age 50 to 17% at age 80. No significant relationship with ischemic heart disease or mortality was found. Men who developed bundle-branch block had a bigger heart volume at age 50 and developed diabetes mellitus and congestive heart disease more often during follow-up than controls. Our results support the theory that bundle-branch block is an indicator of a slowly progressing degenerative disease which also affects the myocardium.

In patients with ischemic heart disease/myocardial infarction, the presence of bundle-branch block has proven to be an indicator of poor outcome. Diagnosis of acute myocardial infarction is difficult when bundle-branch block is present and 12-lead ECG is of limited value especially in patients with left bundle-branch block. We have studied 65 patients with bundle-branch block, admitted to the coronary care unit, with continuous vectorcardiography. In both right and left bundle-branch block changes of the QRS-vector difference during acute myocardial infarction occurred in a similar manner to that in patients with narrow QRS complexes. The evolution of the QRS-vector difference pattern provided additional information for diagnosing acute myocardial infarction in patients with left bundle-branch block. In right bundle-branch block changes of the ST-vector magnitude during acute myocardial infarction occurred in a similar manner to that in patients with narrow QRS complexes. By using ST-vector magnitude >200 μV during the first 4 hours of monitoring as a criterion, a diagnostic accuracy of 83% was achieved for diagnosing acute myocardial infarction in patients with right bundle-branch block. In left bundle-branch block there was no significant difference of ST-vector magnitude in patients with or without acute myocardial infarction.

Previously suggested standard 12-lead ECG criteria for diagnosing acute myocardial infarction were found to be useful in patients with right bundle-branch block but not in patients with left bundle-branch block.

The QRS complex and ST changes of 29 patients with bundle-branch block were studied during elective coronary angioplasty using continuous vectorcardiography. The patients with bundle-branch block were compared to narrow QRS complex controls and matched for the vessel dilated, gender and age. QRS-vector difference, ST-vector magnitude and ST change-vector magnitude responded in a similar way during coronary occlusion in patients with and without bundle-branch block. The study shows that, using continuous vectorcardiography, monitoring of transient ischemia is feasible even in patients with bundle-branch block. For all patients regardless of the presence of bundle-branch block, ST change-vector magnitude is the parameter with best sensitivity for detecting occlusion of a coronary artery.

***Key words**: bundle-branch block, epidemiology, vectorcardiography, electrocardiography, acute myocardial infarction, ischemia.*

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IN PATIENTS WITH BUNDLE-BRANCH BLOCK

by

Peter Eriksson

Göteborg 1998

The value of experience is not in seeing much, but in seeing wisely.

Sir William Osler

To Annika, Clara, Ida, Joel

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CONTENTS

ABBREVIATIONS

ECG:	12-lead electrocardiogram
VCG:	Vectorcardiogram/vectorcardiography
cVCG:	Continuous vectorcardiography
QRS-vd:	QRS-vector difference
ST-VM:	ST-vector magnitude
STC-VM:	ST change-vector magnitude
BBB:	Bundle-branch block
RBBB:	Right bundle-branch block
LBBB:	Left bundle-branch block
NBBB:	No bundle-branch block
LAD:	Left anterior descending artery
LCX:	Left circumflex artery
RCA:	Right coronary artery

INTRODUCTION

Historical background

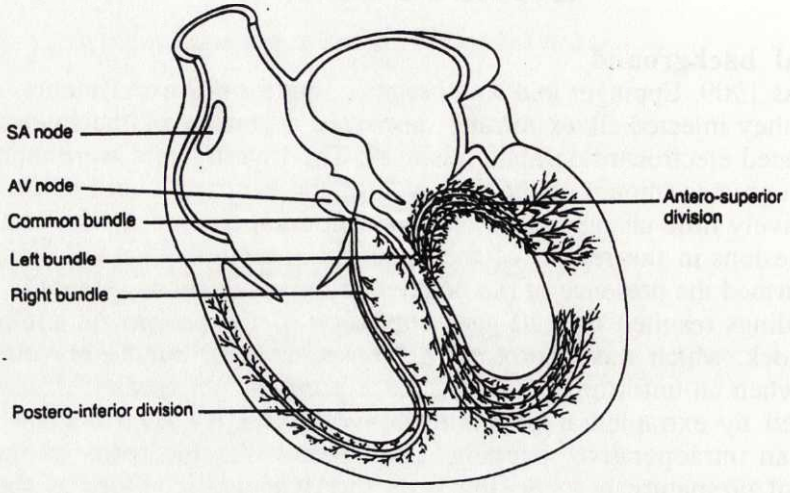
As early as 1909, Eppinger and Rothberger (1) performed experiments in dogs in which they injected silver nitrate, destroyed a portion of the myocardium and produced electrocardiographic changes. The investigators were amazed to find that a greater amount of the free wall of the ventricle could be destroyed with relatively little change in the electrocardiogram compared with the effect of small lesions in the region of the ventricular septum. The following year they confirmed the presence of the bundles of the conduction system (2).
These findings resulted in a 20 year confusion of the pattern of left bundle-branch block, which was incorrectly diagnosed as right bundle-branch block. In 1929 when an unfortunate patient had a purulent pericardial effusion that was treated by extrapleural pericardiostomy, Barker et al. arranged for the first human intraoperative mapping. They found that the form of the QRS complex of premature beats arising from the right and left sides of the heart was quite different from those reported in dogs. As a result they concluded that electrocardiograms that had been regarded as suggestive of right bundle-branch block were, in fact, the result of left bundle-branch block (3). It took several more years for cardiologists to accept this radical revision of their thinking.

Anatomical considerations regarding the distal conduction system

The bundle branches or the branching portion of the AV-bundle begin at the superior margin of the muscular intraventricular septum, immediately beneath the membranous septum, with the cells of the left bundle branch cascading downward as a continuous sheet onto the septum beneath the noncoronary aortic cusp. The AV bundle then may give off other left bundle branches, in some constituting a true bifascicular system with an anteriorsuperior branch. In others it appears more as a network without a clear division into a fascicular system. Irrespective of how much the divisional nature is emphasized, there are multiple connections among these divisions (4, 5). The right bundle branch continues intramyocardially as an unbranched extension of the AV bundle down the right side of the interventricular septum to the apex of the right ventricle and base of the right ventricular anterior papillary muscle.
Although there may be some oversimplification of the trifascicular concept (controversies persist regarding anatomy and function (6)) it has been regarded to have functional utility and allowing meaningful correlation with clinical and electrocardiographic findings (7) (Figure 1).

The histologic characteristics of the Purkinje cells vary depending on where they are found in the conduction system. Generally they are larger and with a higher content of glycogen than working myocardial cells but as they enter the myocardium they become more like the surrounding myocardium.

Figure 1. The conduction system.



Adapted from"Understanding the electrocardiogram" by Derek J Rowlands, Imperial Chemical Industries 1982.

Coronary blood supply

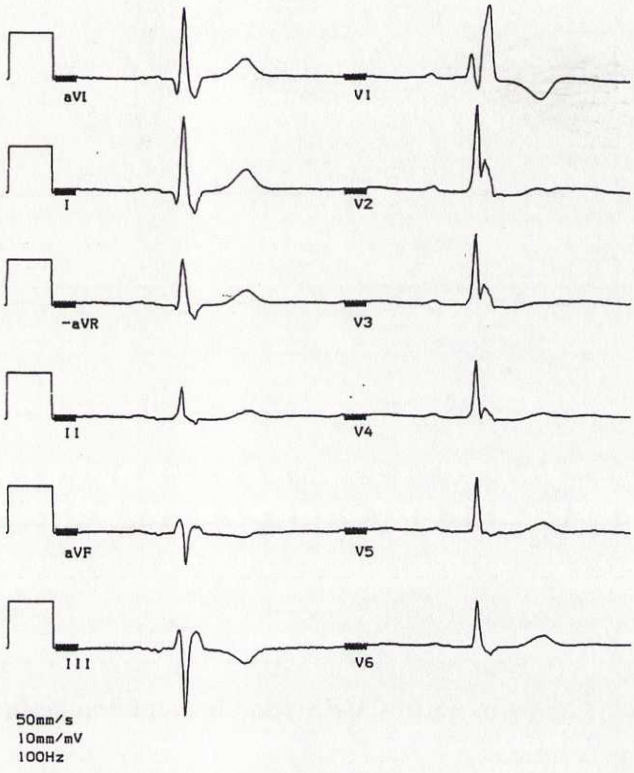
The left bundle branch and its anterior fascicle have a blood supply similar to that of the proximal right bundle branch, that is, from the left anterior descending coronary artery and by the atrioventricular node artery. The posterior fascicle of the left bundle branch receives its blood supply from the atrioventricular node artery and branches from the posterior descending coronary artery and directly from the circumflex artery (8).

Electrocardiography in right bundle-branch block

In right bundle-branch block the QRS duration is ≥120 ms. The initial vector is normally directed to the right and downward, but the terminal vectors, owing to late activation of the right ventricle, are directed to the right, upward and anteriorly. The typical slow terminal portion of the QRS loop forms an appendage directed to the right and anteriorly, whereas the T loop axis is directed opposite to that of the terminal portion of the QRS loop. This gives rise to the typical pattern in V1 with the septal activation inscribing an R wave followed by an S wave reflecting left ventricular activation and a final R wave due to depolarization of the right ventricle from left to right and anteriorly. The depth of the S wave in lead V1 varies depending on whether the left ventricular activation generates a more posteriorly or anteriorly oriented vector and may, in the latter, be very shallow or absent. In lateral precordial leads an initial Q wave (septal depolarization) is followed by an R wave of normal duration and a prolonged, shallow S wave. The T wave is usually inverted in V1-V2, while it is upright in the remaining precordial and limb leads, as a consequence of being opposite directed to the terminal portion of the QRS complex (Figure 2).

Patients with right bundle-branch block and persistent ST elevation in V1-V3 and without obvious structural heart disease have been described as being at risk for sudden death due to malignant ventricular arrhythmias (9, 10).

Figure 2. 12-lead ECG in right bundle-branch block.



Electrocardiography in left bundle-branch block

In left bundle-branch block the QRS duration is ≥120ms. Since the ventricular septum is activated from right to left by way of the functioning right bundle, the initial QRS vector is directed to the left. These initial vectors are the characteristic features of left bundle-branch block and account for the initial positive deflections in the left precordial leads (absence of Q waves). In the horizontal projection, the QRS loop is inscribed as a figure-of-eight directed to the left posteriorly. The loop usually fails to close and the ST vector is directed to the right, anteriorly and inferiorly, resulting in ST elevation in right precordial leads and ST depression in left precordial leads. The T wave is usually oriented at an angle of approximately 180 degrees to the QRS loop;

consequently the T wave is directed opposite of the main deflection of the QRS complex in the electrocardiogram (Figure 3).

Figure 3. 12-lead ECG in left bundle-branch block.

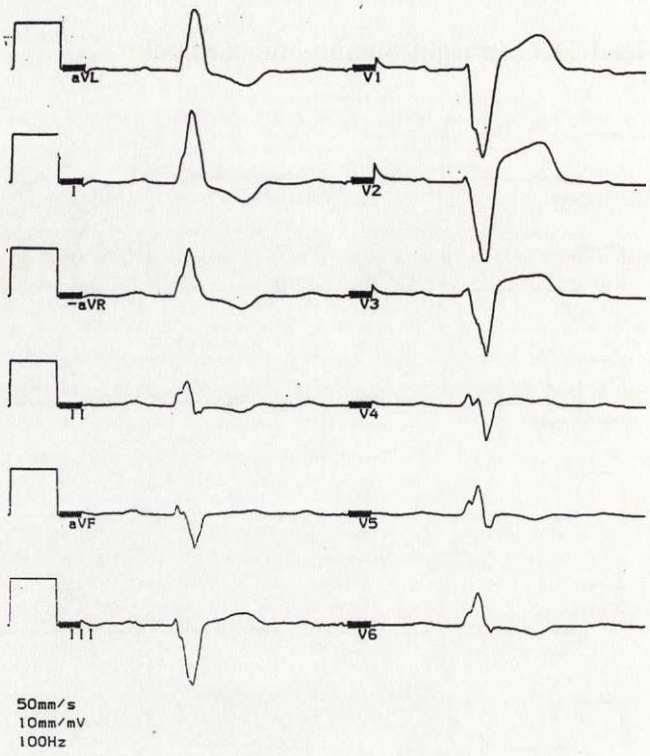
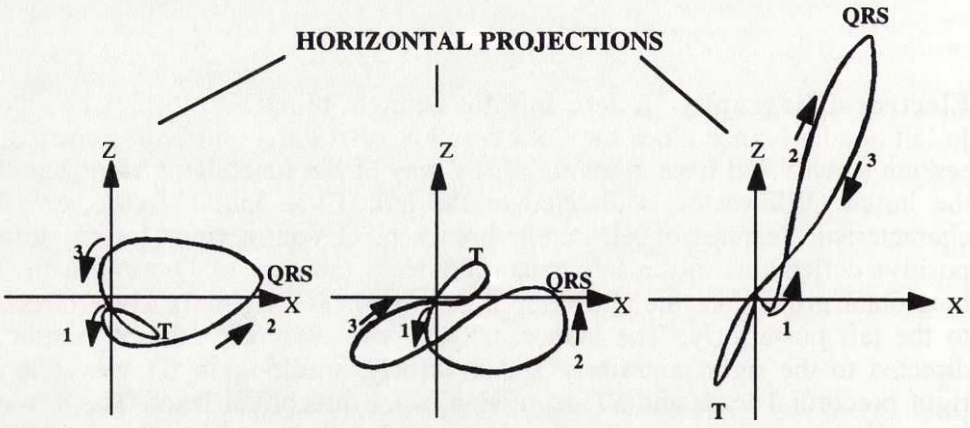


Figure 4. Vector loops in narrow QRS complex and bundle-branch block.



Numbered arrows indicate the directions of the QRS loops. T indicates the T loops.

Theoretical model of electrical activation in bundle-branch block

There is absolutely no way to determine if bundle-branch block is complete or not (11). In fact, one cannot be sure that it is a bundle-branch block at all, only that depolarization occurs as if a bundle-branch was blocked. Not only the sequence of electrical activation but also the direction (endocardium-epicardium), asynchrony of conduction, nonuniformity of refractoriness, changes in membrane responsiveness and probably also changes in the transmembrane action potential, may differ in the presence of bundle-branch block as compared to the absence of bundle-branch block. This gives rise to a wide interindividual and intraindividual variability, making diagnosis of pathological conditions such as myocardial infarction very difficult in the presence of bundle-branch block.

To my knowledge there is today no general theoretical model of the electrical activation that can be used for studying electrocardiographic signs of pathological conditions in the presence of bundle-branch block.

Prevalence of bundle-branch block

The clinical implications of complete bundle-branch block have long been a subject of dispute, partly because of disagreement over its prevalence in the general population. Reports of the electrocardiographic findings among hospitalized patients (12-19), members of the armed forces (20-25), healthy populations on a routine check-up basis (26-29) and other population samples (30-34), have provided important information about prevalence and distribution of certain types of heart disease. It is difficult to assess the differences in frequency of abnormalities reported in such studies due to dissimilarities of the population examined, possible confounding factors and not knowing the prevalence of bundle-branch block in the general community.

In a large screening program, reported by Fahy et al., the prevalence of bundle-branch block was only 0.28%. In the male population over 64 years of age the prevalence was 1.6% (26).The Reykjavik study showed a prevalence of 0.43% for left bundle-branch block among middle-aged men and 0.28% for women (35). For right bundle-branch block the prevalence increased with age, from 0% among men and women 30-39 years of age to 4.1% and 1.6% in men and women, respectively, who were 75-79 years old (36). In a retirement community, the prevalence of bundle-branch block was 3.7%. When considering only the male population at age 52 or above, the prevalence was 5.1% (29). The Tecumseh study showed the prevalence of bundle-branch block to be overall 0.7%, increasing from 0.1% in the 3rd decade to 3.5% in the 8th decade, with no gender difference (37). In the study by Kreger et al., of the Framingham data, complete intraventricular block (defined as QRS ≥120 ms) was strongly dependent on age with a prevalence of 11% in men and 5% in women, in the 8th and 9th decade (38).

Wasserburger studied 396 patients age 75 or older and found the prevalence for left and right bundle-branch block to be 9% and 10% respectively (39).

These studies give a wide range of prevalence, indicating an age relation and possibly a gender dependence.

Pathogenesis of bundle-branch block

The nature of the pathological disturbance in persons with bundle-branch block remains uncertain in any individual case. One can not determine from the electrocardiogram alone whether the conduction disturbance is a function of a focal lesion in the main bundle-branch or the result of a more diffuse myocardial disease producing a type of parietal block. Experimental and clinical studies have lent support to both hypotheses (5, 40-50). In some reports, degenerative changes of the myocardium were widespread, often involving both the right and left bundles (45, 46). Cardiomegaly was common, although large areas of infarction were infrequent (46, 51). In patients with acquired right bundle-branch block, without overt cardiac disease, Lancaster et al. found an unexplained increase in end-diastolic ventricular pressure (52).

In coronary angiographic studies of different populations, bundle-branch block showed a poor correlation to the presence, and the extent, of coronary heart disease (53-56). The presence of bundle-branch block was a poor predictor of coronary heart disease in apparently healthy men (20) or women (57).

Except for ischemic heart disease, there are also reports of cases of intraventricular block in certain other clinical conditions including myotonic dystrophy (58), hyperthyroidism (59), myocardial sarcoidosis (60), "athletic heart" syndrome (61), alcoholic cardiomyopathy (62, 63), Prinzmetal´s angina (64), idiopathic pulmonary hemosiderosis (65) and acute rheumatic carditis (66).

During the first three decades in life, right bundle-branch block is commonly associated with congenital heart disease, especially atrial septal defects (67). Overloading of the right ventricle has been suggested as the cause of right bundle-branch block (68). Finally, rate-related bundle branch block is a well known entity (69-73) but the specific underlying electrophysiological mechanism has been difficult to define.

By reviewing the literature it is hard to link the pathogenesis of bundle-branch block to a certain disease. Whether this indicates multiple causes, or represent a pathogenesis of its own, seems unclear.

Epidemiological evidence for bundle-branch block as a marker for coexisting morbidity

In the Reykjavik study a significant correlation between cardiomegaly and bundle-branch block was found. In right bundle-branch block there was also a correlation between ischemic heart disease and arrhythmias (35, 36). Except for cardiomegaly this was not found in the population of Tecumseh (37). The Framingham data (38, 74) is harder to interpret since it focuses on comparing left to right bundle-branch block, excluding persons without bundle-branch block. However a high prevalence of hypertension, cardiomegaly and ischemic heart disease in persons with bundle-branch block was found. Since bundle-branch block occurred mainly in older age groups, it may reflect the impact of age. For persons with left bundle-branch block both the Reykjavik and the

Framingham study showed a correlation to cardiomyopathy. This is supported by the findings that, 40% had left bundle-branch block, in selected populations of patients with cardiomyopathy (75, 76).

Bundle-branch block as a marker for increased mortality in "healthy" populations

There is considerable information in the literature indicating that persons with bundle-branch block, either right or left, may have normal longevity (16, 25-28, 77-79). In the Framingham Study, an increased mortality from cardiovascular disease was reported in subjects with bundle-branch block. However, the overall mortality rate was not given (74).

Bundle-branch block as a marker for increased mortality in myocardial infarction/ischemic heart disease

In studies of acute myocardial infarction, bundle-branch block has proven to be a strong predictor of high mortality both in the hospital and during follow-up (80-93). Some studies have demonstrated a lower mortality in patients with left bundle-branch block than in patients with isolated right bundle-branch block or bifascicular block involving the right bundle-branch (80, 94, 95). Other studies have demonstrated equal or higher mortality with left bundle-branch block (83, 86, 90, 96-98).

From the Coronary Artery Surgery Study (CASS) which angiographically studied over 15,000 patients, 522 were identified with bundle-branch block. The two-year mortality was five times higher for left bundle-branch block and two times higher for right bundle-branch block, independent of the extent of the coronary artery disease (99).

Patients with preexisting bundle-branch blocks might be expected to have a lower mortality than patients who develop this condition during an acute myocardial infarction. This can be explained by the fact that the development of bundle-branch block indicates more extensive myocardial damage in the latter patients. This effect of the onset of bundle-branch block on mortality was demonstrated in two studies (100, 101), while other investigators have not found that the age of the bundle-branch block significantly influences mortality (85, 86, 91).

Several investigators have found that the onset of bundle-branch block during acute myocardial infarction is indicative of ischemia in the area supplied by the left anterior descending artery (86, 90, 91, 97, 102). In the CASS registry, no particular location of coronary artery stenosis or left ventricular wall motion abnormality predominated in patients with bundle-branch block (99).

The overall importance of bundle-branch block as an indicator of poor outcome in patients with acute myocardial infarction has not changed in the thrombolytic era (100, 102, 103). The poor prognosis for patients with the combination of bundle-branch block and myocardial infarction is related infarct size and the development of left ventricular dysfunction. Moreover, the incidence of sudden death after a myocardial infarction is increased, indicating

that late bradyarrhythmias and electric instability might be as important (14, 104).

Arrhythmias in patients with bundle-branch block

The overall annual incidence of progression to high degree atrioventricular block in an unselected population of patients with bundle-branch block is 1% to 4% (104-106).

Pacemaker treatment has not been found to diminish the risk of sudden death in patients with bundle-branch block (14, 105, 107). In a large sample of patients with chronic pacemaker treatment, bundle-branch block was an independent risk factor predicting sudden death (108).

During acute myocardial infarction atrioventricular block has been found to be more common in patients with bundle-branch block (85, 86, 100, 103) but prophylactic pacing did not reduce the high hospital (109), or two year mortality (110).

The role of bradyarrhythmias and high degree atrioventricular block does not seem to have a major impact on mortality, indicating that malignant tachyarrhythmias are more important. This hypothesis is supported by studies of patients with ventricular fibrillation who had an unexpected high prevalence of bundle-branch block (111, 112). In a study by Watson et al., patients with bundle-branch block treated prophylactically with pacemakers were found to have a high mortality, mostly due to ventricular fibrillation (110).

Diagnosis of myocardial infarction in the presence of bundle-branch block

Standard 12-lead ECG

One cornerstone in diagnosing acute myocardial infarction in patients with narrow QRS complex is the changes in ST-T waves by standard 12-lead ECG. In patients with bundle-branch block, as previously described, there are "secondary ST-T wave changes". Thus they may be secondary to the bundle-branch block and may not indicate any other cardiac disease. This fact makes the diagnose of myocardial infarction, in the presence of especially left bundle-branch block, difficult.

Numerous attempts have been made to determine which ECG patterns indicate the presence of myocardial infarction/ischemia when superimposed on the QRS, ST, and T wave changes that normally are present in bundle-branch block. In some studies autopsy findings have been compared with prior ECG changes (113-117), other have looked at patients with myocardial infarction and intermittent bundle-branch block (118-120), and some have compared the ECGs of patients with "uncomplicated bundle-branch block" against the ECGs of patients with bundle-branch block and myocardial infarction as diagnosed by clinical findings and laboratory data (121-125).

Several studies have shown a high prevalence of pathologic Q waves in patients who were diagnosed either clinically, or at autopsy, as having bundle-branch

block complicated by myocardial infarction (114, 118, 121, 122, 124, 126). However, others have shown in clinical and pathological studies that the appearance of pathological Q waves is neither a sensitive nor a specific indicator of the presence of myocardial infarction in patients with bundle-branch block (116, 117, 119, 120).
It seems clear, that changes in the ECG do occur as a result of myocardial infarction, but in a complex way with many variations. Only a few criteria have been shown to be useful when tested prospectively, all with a very low sensitivity for diagnosing myocardial infarction (125). Importantly, most studies have not attempted to separate acute, ongoing myocardial infarction from old prior infarction. There are various problems attached to studying prior myocardial infarction, e.g., the risk of inaccurate histories, selection bias, false-positive results from thallium scintigraphy, difficulties in interpretation of wall motion abnormalities, interpretation of clinically insignificant stenosis in coronary arteriograms, and, retrospective ECG evaluation for the presence or absence of myocardial infarction.
There are to my knowledge only two studies that have focused on diagnosing acute myocardial infarction when left bundle-branch block is present (125, 127). The study by Sgarbossa et al. (127) is the only one exclusively looking at ECG changes in acute myocardial infarction in the presence of left bundle-branch block. Retrospectively from the GUSTO database they selected criteria for indicating ongoing myocardial infarction from one single admission 12-lead ECG. The results were promising, and the criteria suggested have gained wide acceptance, even though the criteria have never been tested in a clinical setting, except for the published validation sample of 45 patients.

When right bundle-branch block is complicated by acute myocardial infarction, the ST segment and T waves reflect marked changes which are primary in character, and the direct result of the acute myocardial ischemia. These changes supposedly have the same characteristics as when they occur in association with acute myocardial infarction not complicated by right bundle-branch block (128). This has, to my knowledge, never been validated but questioned (129).

Other electrocardiographic techniques
It has been shown that serial comparison of consecutive ECGs improves diagnostic accuracy, mainly due to improved sensitivity (130). In comparative studies vectorcardiography has been shown to be more accurate than standard ECG in detecting prior myocardial infarction in patients with left bundle-branch block (131, 132).
By performing an analysis of changes in the entire QRST-complex using QRST integral maps in simulated left bundle-branch block (133, 134), and in "true" bundle-branch block (135, 136), an improved diagnostic accuracy of prior myocardial infarction in patients with left bundle-branch block has been reported. Recently, Menown et al. reported on the use of body surface vector mapping (137). The method correctly identifyied 6 of 8 patients with acute

myocardial infarction in the presence of left bundle-branch block, with a specificity of 91%.

Continuous vectorcardiography
Dynamic vectorcardiography has been used in clinical trials of acute myocardial ischemia and infarction (138-147), and also in animal studies (148-151). In patients with narrow QRS complexes computerized, dynamic vectorcardiography has been shown to be a valuable tool in diagnosing acute myocardial infarction by trend analysis of QRS-complex and ST-segment changes (138, 139). However, there are no reports on its use in patients with bundle-branch block.

Transient ischemia in the presence of bundle-branch block
The presence of transient ischemia in the unstable coronary syndrome is associated with increased risk for mortality and nonfatal myocardial infarction in the near future (152-154). Moreover, by analyzing the presence and number of ST episodes during the first 24 hours after admission of patients with unstable angina and normal QRS complex, it is possible to predict the 7-day and one-year outcome (155, 156). The information about transient ischemia detection in the presence of bundle branch block is limited (157, 158). Today angioplasty is a well established method for treatment of coronary stenosis, but it is also an interesting model for studying transient myocardial ischemia resulting from coronary occlusion.
Continuous vectorcardiography (cVCG) has been used to study patients with narrow QRS complex during angioplasty (141, 159), and cVCG has been shown to have a higher sensitivity than ECG (160).
Stark et al. have previously shown that ST segment analysis is feasible in patients with left bundle branch block using digital self referenced ST analysis during angioplasty (157).

Detection of ST changes with cVCG and changes of the QRS complex have not previously been reported in patients with bundle-branch block during transient ischemia.

AIMS OF THE PRESENT STUDY

The aims of the present study were:

* to describe the prevalence and cumulative incidence of bundle-branch block in a general male population,

* to investigate the impact of bundle-branch block on survival in a general male population,

* to study the correlation between bundle-branch block and ischemic heart disease,

* to give a description and diagnostic evaluation of the use of continuous vectorcardiographic monitoring during acute myocardial infarction in patients with bundle-branch block,

* to evaluate standard 12-lead ECG criteria for diagnosing acute myocardial infarction in patients with bundle-branch block, and,

* to describe continuous vectorcardiographic changes during coronary angioplasty in patients with bundle branch block compared to patients with narrow QRS complex.

METHODS

Subjects

Paper I

The "Study of Men Born in 1913" is a longitudinal prospective study of men born in 1913, and living in the city of Göteborg on the west coast of Sweden (161). In 1963, Göteborg had approximately 500,000 inhabitants. All residents in Sweden have a unique national ten-digit registration number based on their date of birth. The County Census Bureau is required by law to keep registration numbers, names and addresses up-to-date in an official register. In 1963, a sample was drawn from the population register consisting of all men born in 1913 on a day divisible by three (i.e., the third, sixth, ninth day and so on, of each month) and living in the city of Göteborg. These criteria were fulfilled by 973 men, 855 (88%) of whom agreed to participate in a health examination. From the baseline examination in 1963, when all the men were 50 years old, 855 men have been followed for 30 years with repeated examinations (in 1967, 1973, 1980, 1988, and 1993).

The participants and non-participants have previously been described in detail (162-164).

Systematic 12-lead ECG recordings were made in 1963, 1980, 1988 and 1993 and form the basis of the present study (Table 1). All ECGs have retrospectively been read by the author, blinded to all data, and classified as to whether bundle-branch block was present or not.

Left bundle-branch block was defined as; 1) QRS duration ≥120 ms; 2) PQ interval >120 ms; 3) predominantly upright complexes with slurred R waves in lead I, V5 and V6, and; 4) QS or rS pattern in V1.

Right bundle-branch block was defined as; 1) QRS duration ≥120 ms; 2) PQ interval >120 ms; 3) rSR´ in lead V1 or V2, and; 4) S waves in lead I and either lead V5 or V6.

If atrial fibrillation was present, the ECG was still included as a bundle-branch block even though the criterion of PQ interval >120 ms could not be fulfilled. All patients with a QRS duration ≥120 ms have been classified as either right or left bundle-branch block after considering the possibility of electrode displacement and variations of position of the heart.

During the four examinations, 82 men with bundle-branch block were found and were compared to men without bundle-branch block.

Paper II-IV

All patients admitted to the coronary care unit at Östra University Hospital, Göteborg, from September 1988 to December 1991, who presented with clinical suspicion of ongoing acute myocardial infarction and bundle-branch block were available for inclusion. The coronary care unit serves a population of 250,000 inhabitants and consisted at that time of six beds with the possibility of continuous vectorcardiographic monitoring in three of the six beds. During

the time period there were a total of 5,206 admissions of whom 1,733 had an acute myocardial infarction diagnosed. Seventy-seven patients, 1.5% of all admissions, were included and monitored. Twelve patients were excluded from further analysis: five did not fulfill the criteria of bundle-branch block; four had only intermittent bundle-branch block; and, three for technical reasons. Thus 65 patients were left for analysis according to the protocol, and form the basis of the study in *Paper II.*

Of the 65 patients described in *Paper II,* 23 had right bundle-branch block and all of them had a standard 12-lead ECG taken at admission and 12-24 hours after admission, and were studied according to the protocol in *Paper III.*

Of the initial 42 patients with left bundle-branch block and who had completed vector cardiographic recordings, nine did not have a standard 12-lead ECG taken 12-24 hours after admission and were excluded, leaving 33 patients to be studied in *Paper IV.*

Table I. Study population in *Paper I.*

Year	Possible participants	dead or lost to follow-up*	No ECG available	In the study with ECG available
	(n)	(n)	(n)	(n)
1963	855	-	1	854 (99,9%)
1980	697	158	130	567 (81%)
1988	518	337	123	395 (76%)
1993	361	494	149	212 (59%)

Possible participants= All men alive and not lost to clinical follow-up.
Dead or lost to follow-up= Cumulative numbers are shown.
No ECG available= at that particular examination.
*A total of 13 patients (1.5%) were lost to clinical follow-up over the 30-year follow-up period.

Paper V
Thirty-five patients, who had chronic bundle-branch block and were scheduled for routine coronary angioplasty between May 1995 to December 1997, at Sahlgrenska University Hospital, were studied. Patients available for inclusion in the study were patients with bundle-branch block who were scheduled to undergo elective angioplasty for stable angina pectoris or semiacute angioplasty for unstable angina. Patients with ongoing acute myocardial infarction, closed target vessel, or intermittent bundle-branch block were not considered.
One patient had an acute closure and 5 patients had their average time period set to 1 minute, instead of the requested 10 seconds. These 6 patients were excluded from further analysis. From an earlier study by Dellborg et al. on 114 patients during coronary angioplasty with narrow QRS complex (159), controls were selected that matched for 1) the coronary vessel dilated, 2) gender, and 3) age.
Paper V thus reports on the findings from 29 patients with bundle-branch block and their matched controls with narrow QRS complex.

Epidemiological variables *(Paper I)*
The variables studied were; medical history data, physical findings, anthropometry, blood chemistry, X-ray findings, morbidity, and mortality, at baseline and during follow-up. In most instances, generally accepted standard methods and questionnaires were used. To be practical in an epidemiological study, a method must be simple and cheap enough to be employable on a large scale and also safe enough to be used in apparently healthy individuals. It must be accurate both as to the precision of the estimate and to the extent to which the method measures what it is supposed to measure. The methods in this study were selected as far as possible according to these criteria and are described in detail in *Paper I*. The participants were examined at the same time of the day on each occasion. They followed the same time schedule and underwent the investigations in the same order. The examinations were performed over the year with a break from the middle of June to the middle of August. The possible bias caused by examining individuals in different seasons during the study might be counteracted by the break, since the seasonal variation is most extreme during this period. The bias due to seasonal variation is probably small and has an effect only on the blood pressure variability. To reduce the observer error, the number of observers was kept as low as possible.

Morbidity, mortality and follow-up
Informations about hospitalization, medication and morbidity since the previous examination were obtained at each examination.
Diabetes mellitus was defined as known diagnosis of diabetes mellitus under treatment or fasting blood glucose $\geq$ 6.7 mmol/L.
Myocardial infarction was defined as by the criteria of the Swedish Society of Cardiology or post mortem findings of fresh coronary heart disease.

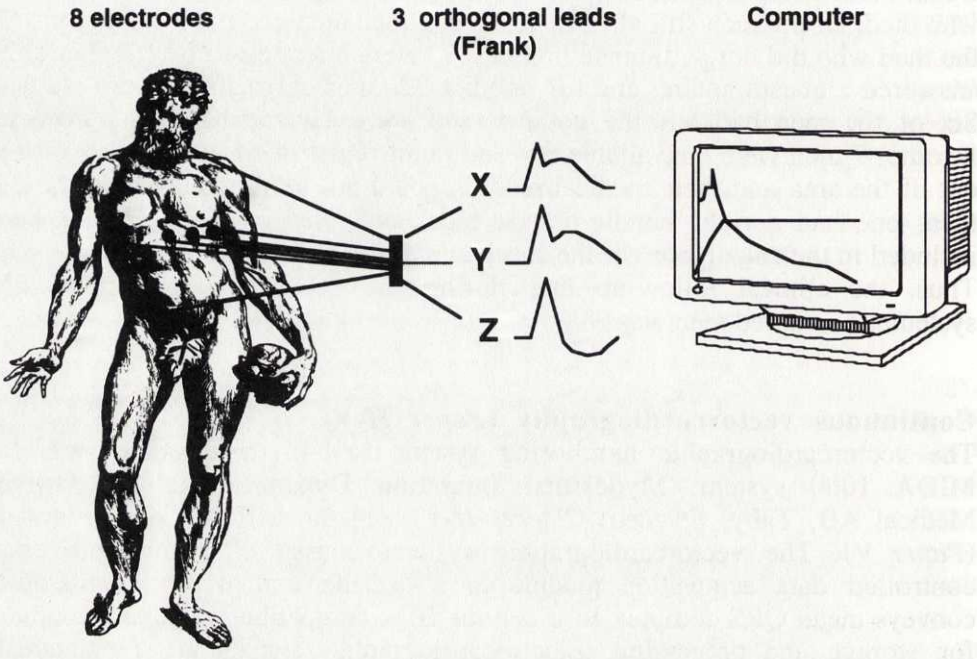
Ischemic heart disease, was defined to include myocardial infarction, and additionally included hospitalization due to angina pectoris/unstable angina pectoris, and suspected acute myocardial infarction.
Congestive heart failure was defined as hospitalization for heart failure or out-patient treatment for heart failure for at least 3 months.

Death certificates, autopsy reports and medical records were studied for those who died. By 1993, after 30 years of follow-up, 481 men (56.3%) had died. Death certificates and medical reports could be found for all but 2 of those who died. Of the men still alive in 1993, 232 men attended the examination. Of the men who did not participate in 1993, 67 were interviewed by telephone, 29 answered a questionnaire, and for another 32, medical records were studied. Six of the men had left the country and were unavailable for follow-up. Another 7 men were unavailable for end point registration as they had moved out of the area and their medical records could not be found. Among these 7 men, one had a right bundle-branch block and died in 1995. He has been included in the calculation of the survival data.
Thus, the clinical follow-up rate during the 30-year follow-up of 855 systematic sampled men was 98%.

Continuous vectorcardiography (*Paper II-V*)
The vectorcardiographic monitoring system used in these studies was the MIDA 1000 system (Myocardial Infarction Dynamic Analysis, Ortivus Medical AB, Täby, Sweden) (*Papers II-V*) and the MIDA Coronet system (*Paper V*). The vectorcardiographic systems consist of a microprocessor controlled data acquisition module in a bedside unit which continuously conveys mean QRS complex to a central IBM compatible personal computer for storage and processing. Electrocardiographic signals are continuously collected from conventional body surface electrodes applied to the patient according to the Frank lead system (165). The Frank lead system allows for three dimensional reconstruction of electrocardiographic complexes and these are displayed in the three orthogonal planes X, Y, and Z. The sensitivity of the system is 1 μV and the sampling rate is 500 Hz. The storing rate is 500 Hz in the MIDA 1000 system and 250 Hz in the MIDA Coronet system. The electrocardiographic signals are classified according to their shape into one of five classes. The most dominant QRS shape is determined during the first 10 seconds of recording and automatically termed the zero class. After acceptance of the operator, or selection of any other QRS complex class displayed, the system uses the zero class for all subsequent analysis and beats with a different morphology are subsequently discarded. The vectorcardiographic signals are sampled over time periods of 2 minutes (*Paper II-IV*) or 10 seconds (*Paper V*). Averaging is performed for consecutive periods, for each sampling period a mean complex is computed and compared with the mean complex recorded from the second averaging period. Changes in several parameters can be followed as trend curves, which are continuously up-dated and displayed on

the central color monitor for on-line interpretation. At any time a derived 12-lead ECG can be presented on the computer screen and give an account of any deflection of the trend curves. Also, vector loops for the P, QRS, and T waves can be studied.

Figure 5. Continuous vectorcardiography (cVCG).



Analysis and clinical handling

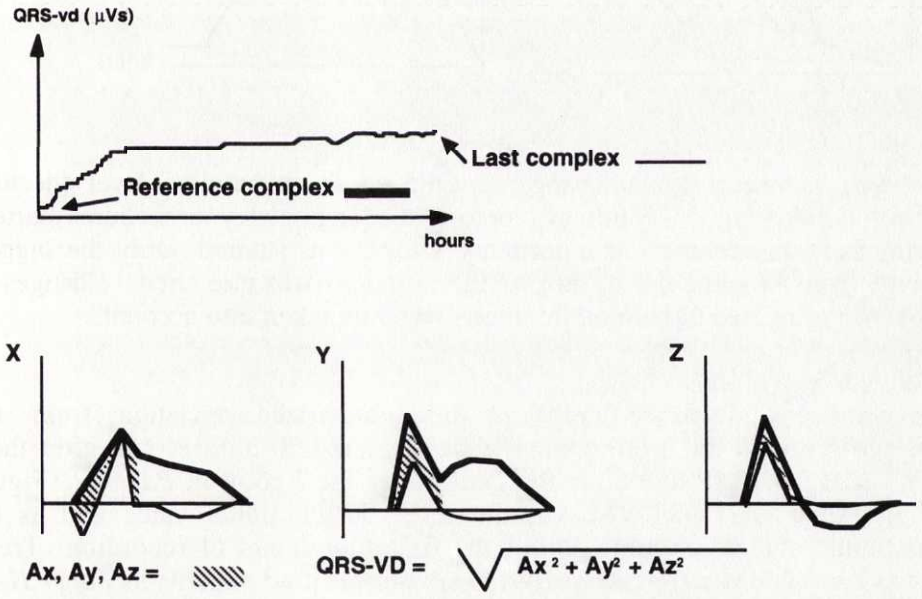
In *Paper II-IV*, the patients were in supine position most of the time but no strict recording of body position was made. Monitoring began immediately on arrival of the patient in the coronary care unit but there was no time limit from onset of chest pain until admission. All patients were monitored for at least 12 hours. All patients were treated according to the standard routines regarding the use of thrombolysis, intravenous nitroglycerin, beta blockade etc. The trend curves were visible on a computer screen in the coronary care unit but clinical decision making as well as diagnosing from interpretation of the trend curves was strongly discouraged. During the time period when the recordings were done (1988-1991) there were no guidelines whatsoever available. All analyses were done retrospectively from diskettes with the observers blinded to all clinical information. Disagreements were solved by consensus.

In *Paper V* the patients were in supine position all the time and monitored while in the catheterisation laboratory. During the whole procedure patient information was written in a separate file, indicating the exact time for contrast media given, time of balloon inflation, segment of the coronary artery occluded and information on what balloon type, size, maximum pressure and if any additional device (e.g. stent) was used. The file with patient information was then used as a "manuscript" when retrospectively analyzing the trend curves in order to identify changes caused by guide positioning and administration of contrast media, giving the possibility to focus on changes seen only during balloon occlusion of the coronary artery. All recordings have been analyzed by the author.

QRS-vector difference

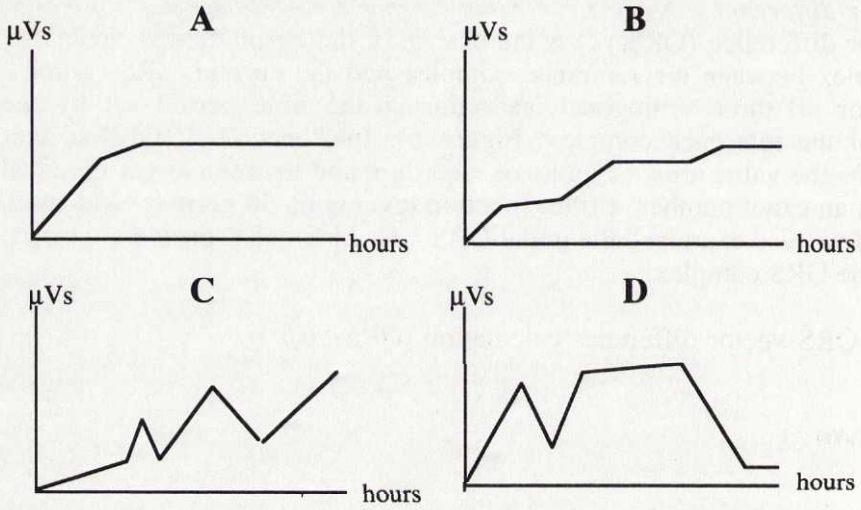
QRS-vector difference (QRS-vd) is the change in the absolute area under the QRS complex between the reference complex and the current QRS complex summed for all three orthogonal leads during the time period set by the duration of the reference complex (Figure 6). In *Paper II-IV* QRS-vd was measured as the value after 12 hours of recording and in order to get the level rather than an exact number, a filter function (averaging 50 periods) was used. In *Paper II* we also examined the initial QRS-vd which only considers the first 40 ms of the QRS complex.

Figure 6. QRS-vector difference calculation (QRS-vd).



Trend curves for QRS-vd were categorized in four prespecified patterns based on the reports by Dellborg et al. (138) in studies of patients with narrow QRS complex and acute myocardial infarction (Figure 7). Pattern A is a rapidly increasing pattern reaching a plateau. Pattern B is an irregularly increasing pattern reaching a plateau late (>8 hours). Pattern C is an irregularly increasing pattern not reaching a plateau. Pattern D is an irregularly pattern that is not changing consistently from the initial level. It also includes a stable trend with only minor alterations.

Figure 7. Categorized QRS-vd patterns.



In *Paper V,* the maximal change of QRS-vd from baseline level (decided during monitoring 5-15 minutes before the angioplasty procedure started) during balloon occlusion of a coronary artery, was studied. Only the biggest change from baseline during any of the inflations was measured. Changes of QRS-vd not related to balloon inflations were not taken into account.

ST-vector magnitude

ST-vector magnitude (ST-VM) is the summarized deviation from the isoelectric line in the 3 orthogonal leads measured 20 milliseconds after the J point in *Paper II-IV* and 60 milliseconds after the J point in *Paper V* (Figure 8). In *Paper II-IV,* ST-VM was measured as the initial value and as the maximum value at any time during the first four hours of recording. Trend curves for ST-VM were categorized in six prespecified patterns in *Paper II-IV* based on the reports by Dellborg et al. (138) and Näslund et al. (166) in studies of patients with narrow QRS complex and acute myocardial infarction (Figure 9). Pattern A is a rapidly declining pattern reaching a plateau. Pattern B is the

same as for A adding the presence of a "reperfusion peak". Pattern C is a rapidly declining pattern with a plateau with additional ST-VM episodes. Pattern D is an irregular pattern with no obvious direction (inclining/declining). Pattern E is a stable pattern with only minor alterations (<50 μV), and pattern F is an irregular pattern with several baselines and episodes.

In *Paper V* the maximal change of ST-VM from baseline level (decided during monitoring 5-15 minutes before the angioplasty procedure started), during balloon occlusion of a coronary artery, was studied. As for QRS-vd only the biggest change during any of the balloon inflations was considered.

Figure 8. ST-vector magnitude (ST-VM).

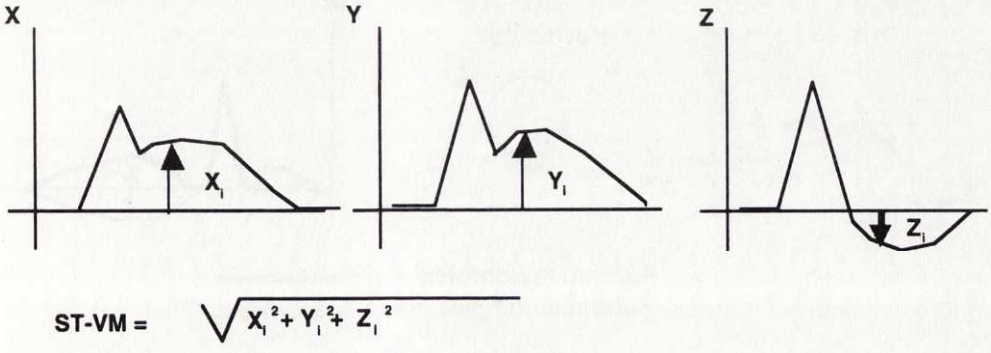
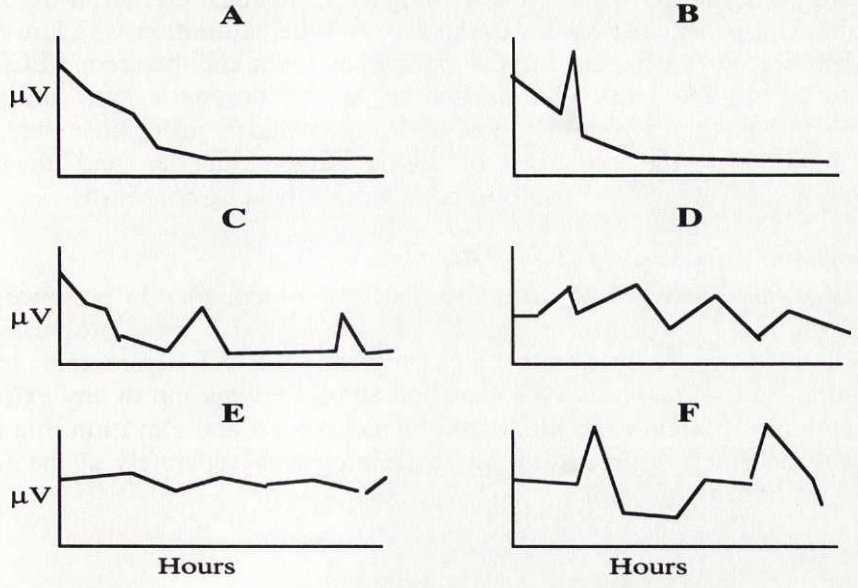
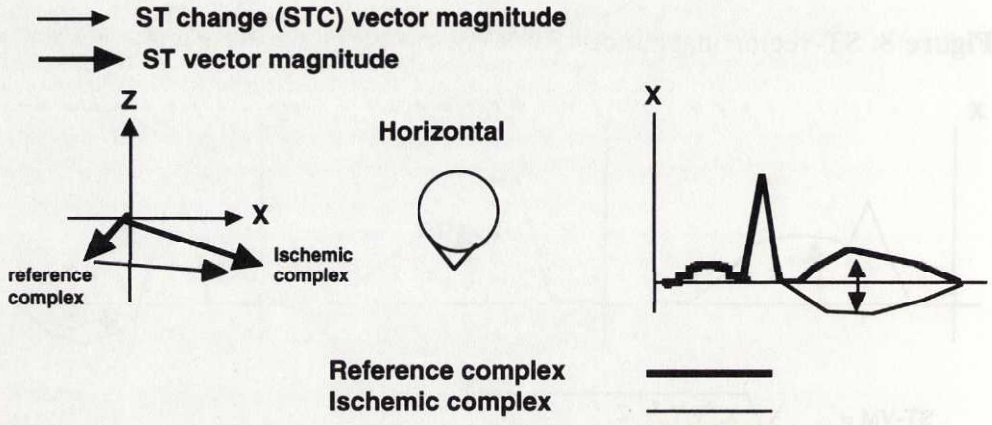


Figure 9. Categorized ST-VM trend patterns.



ST change-vector magnitude
The ST change-vector magnitude (STC-VM) is the length of the difference-vector between the initial (reference) ST vector and the current ST vector in three dimensions (Figure 10) measured 60 milliseconds after the J point.
In *Paper V* the maximal change of STC-VM from baseline level (decided during monitoring 5-15 minutes before the angioplasty procedure started), during balloon occlusion of a coronary artery, was studied.

Figure 10. ST change-vector magnitude (STC-VM).



Standard 12-lead ECG criteria for acute myocardial infarction
Standard 12-lead ECG was recorded (Megacart, Siemens-Elema) in the supine position. The paper speed was 50 mm/sec, and the calibration was 1 mV : 10 mm. The first ECG was taken in the emergency room and the second ECG was taken after 12-24 hours of observation at the coronary care unit. The recordings were retrospectively analyzed by two independent observers, who were blinded to the sequence of ECG, patient identity and diagnosis. Disagreements between the two observers were solved by consensus.

Right bundle-branch block (Paper III)
All ECGs were analyzed according to a strict protocol for; 1) presence of Q waves >30 ms; 2) presence or absence of pathological R wave progression in precordial leads; 3) maximum ST elevation and ST depression in any precordial lead; 4) maximum ST elevation and ST depression in any extremity lead; and, 5) electrical axis. Maximum ST depression and elevation in a single lead was measured in precordial and extremity leads separately at the J-point and 80 ms after the J-point.

Left bundle-branch block (Paper IV)
All ECGs were analyzed according to a strict protocol for; 1) presence of ST depression ≥1mm in V1-V3; 2) any ST elevation ≥1 mm, concordant to the QRS complex; 3) any ST elevation ≥5 mm at the j-point, discordant to the QRS complex; 4) T wave concordant to the QRS complex; 5) maximum ST elevation and ST depression in any precordial lead; and, 6) maximum ST elevation and ST depression in any extremity lead.
Maximum ST depression and elevation in a single lead was measured in precordial and extremity leads separately at the J-point and 80 ms after the J-point.

Clinical diagnosis of acute myocardial infarction *(Paper II-IV)*
In the presence of bundle-branch block a diagnosis was based on a typical history and elevation of myocardial enzymes. Enzyme criteria were based on the clinical routine at that time in our hospital. Two values above the criterion for myocardial infarction were needed to be judged as an acute myocardial infarction. Either two of the same kind or the combination, depending on the time window. Total creatine kinase was available for all but one patient. In 53 patients, analysis of the mass concentration of the MB fraction (167) was made. The cutoff values were creatine kinase MB >20 μg/L or creatine kinase MB (IMX) >15 μg/L, depending on assay used.
In 10 patients with elevated total creatine kinase, the creatine kinase B-activity was analyzed. A value ≥0.2 μkat/L was considered to be of cardiac origin. Total lactate dehydrogenase (168) was analyzed in 57 patients. Total lactate dehydrogenase >8 μkat/L with isopattern 1 and 2 or quantification of lactate dehydrogenase-1 >3.3 μkat/L was used for indicating acute myocardial infarction (169).
In one patient the diagnosis of acute myocardial infarction was based only on the combination of elevated total lactate dehydrogenase and a transient elevation of aspartate aminotransferase.

Coronary angioplasty *(Paper V)*
The number of inflations, occlusion time, and the use of additional device were at the discretion of the interventional cardiologist. All patients had a successful procedure, defined as a residual stenosis less than 50%.

Ischemia criteria *(Paper V)*
Both QRS-vd and ST-VM have been used as ischemia markers during angioplasty in patients with narrow QRS complex (141). In the study by Jenssen et al. STC-VM >50 μV was shown to be the most sensitive criterion for ischemia in patients with narrow QRS complex during angioplasty (160).

Statistics

In *Paper I,* the study group consisting of the subjects with bundle-branch block was compared with the rest of the population with available ECGs. For differences between groups, Wilcoxon Rank Sum test was used for continuous variables and Chi-square test was used for differences in proportions. A life table method according to Kaplan-Meier (170) was used to calculate the survival curves and the cumulative incidence for bundle-branch block. The cumulative incidence was based on those still alive and available to follow-up with regards to ECGs. Men with a bundle-branch block were not considered at risk the next year.

In *Paper II-V,* distribution of continuous variables are shown as boxplots, where horizontal lines display the 10th, 25th, 50th, 75th and 90th percentiles. The Mann-Whitney U test was used for comparison between groups. Discrete variables were compared with Chi-square with continuity correction or Fischer´s exact, as appropriate.
Simple regression was used for correlation of enzymes and QRS-vector difference in *Paper II.*
Univariate analysis of five year mortality was performed by the log rank test, then a stepwise Cox regression was performed incorporating all variables with a univariate p value less than 0.05 to identify independent predictors for mortality in *Paper IV.*

All p values less than 0.05 were considered significant. Calculations were performed using SAS statistical software, SPSS (Statistical Package for the Social Sciences, Pittsburgh, USA) or Statview 4.5 for Macintosh.

Ethical considerations

The study protocols for *Paper I* and *V* were approved by the ethics committee of Göteborgs University. In 1988 when the protocol of *Paper II-IV* was written, this kind of observational study did not need any local ethical committee approval. Recently, a Swedish multicenter study with a very similar protocol has been conducted with the approval of all local ethics committees. All patients in the studies have given their informed consent to participate.

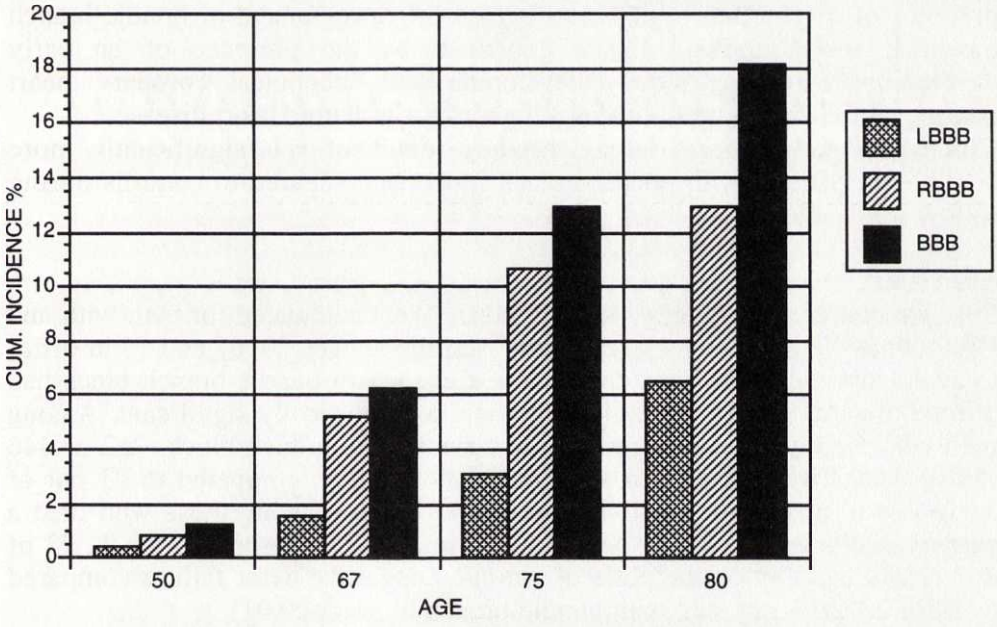
RESULTS

Prevalence and cumulative incidence in a general population

During follow-up of 855 men from age 50 to age 80, a total of 82 men with bundle-branch block were found. The prevalence of bundle-branch block was found to increase with age, from 1.2% to 17% during the follow-up period. The result was a cumulative incidence of 18.1%, showing that almost every fifth man at age 50 living till the age of 80 will develop bundle-branch block. Right bundle-branch block was found to be more common than left with the overall ratio of 3:1, and ranging from 4:1 at age 75 to 2:1 at age 80 (Figure 11).

During the follow-up period, 60 men were found with right bundle-branch block and 22 with left bundle-branch block. Bundle-branch block was acquired after the age of 50 in 87% of all cases.

Figure 11. Cumulative incidence of bundle-branch block.



Relation to ischemic heart disease

The exact prevalence of ischemic heart disease in a general population is hard to estimate without repeated coronary arteriograms at different ages. This is especially true when bundle-branch block is present, since advanced ischemic heart disease could be present without clinical manifestations.

In order to avoid inaccurate histories and selection bias we focused on describing the likelihood of ischemic heart disease as; 1) the difference in risk factors for ischemic heart disease at age 50; 2) the incidence of hospitalization due to acute myocardial infarction, unstable angina pectoris or suspected acute myocardial infarction during follow-up; and, 3) the incidence of cardiovascular death in men with bundle-branch block compared to men with no bundle-branch block. When adjusted for age and survival by analyzing survivors at ages 67, 75 and 80 separately we found no significant differences in any of the above described variables except for developing diabetes during follow-up which was more common in men with bundle-branch block (Table II).

Bundle-branch block as a marker of a slowly progressive degenerative myocardial disease

The heart volume at age 50 was consistently larger among those who developed bundle-branch block (the majority had not developed a bundle-branch block at the time of X-ray in 1963) compared to controls. This difference was consistent when considering survivors at age 67 as well as at age 75, but not significant at age 80 (Table II). This finding indicates the presence of myocardial engagement before the development of bundle-branch block. It seems unlikely to be explained by the presence of an early developing, extensive, slowly developing and subclinical coronary heart disease not related to traditional risk factors for ischemic heart disease.

Clinical congestive heart failure needing treatment was significantly more common in patients with bundle-branch block as compared to controls during follow-up (Table II).

Survival

Survival curves according to Kaplan-Meier were calculated for men with and without bundle-branch block separately starting at ages 50, 67 and 75 in order to avoid survival bias. On all three curves, men with bundle-branch block had a trend towards higher mortality, although not statistically significant. Among men who died without being known to have bundle-branch block, 262 of 446 (59%) deaths were diagnosed as being cardiovascular, compared to 23 out of 35 (66%) in men with bundle-branch block (p=ns). Among those who died a cardiovascular death without being known to have bundle-branch block, 73 of 262 (28%) had a prior diagnosis of chronic congestive heart failure compared to 14 of 23 (61%) in men with bundle-branch block ($p<0.01$).

Table II. Baseline risk factors at age 50 and end points during follow-up, in survivors at different ages, in men with as compared to without bundle-branch block.

	Survivors at age 67				Survivors at age 75				Survivors at age 80			
	RBBB n=28	LBBB n=8	BBB n=36	No BBB n=531	RBBB n=39	LBBB n=9	BBB n=48	No BBB n=347	RBBB n=24	LBBB n=12	BBB n=36	No BBB n=176
At age 50:	mean	mean	mean	mean	mean	mean	mean	mean	mean	mean	mean	mean
Systolic BP (mmHg)	135	144	137	137	139	142	140	136	134	144	137	135
Diastolic BP (mmHg)	92	92	92	91	93	94	93	90	91	96	93	89
B-Glucose (mmol/L)	4.4	5.3	4.7	4.6	4.6	4.7	4.6	4.6	4.6	4.6	4.6	4.6
S-Cholesterol (mmol/L)	6.4	6.3	6.4	6.4	6.3	6.1	6.3	6.4	6.1	5.9	6.1	6.3
S-Triglycerides (mmol/L)	1.3	1.1	1.3	1.2	1.4	1.1	1.3	1.2	1.2	1.0	1.1	1.2
Body mass index (kg/m^2)	25.6	25.1	25.5	24.8	25.1	24.0	24.9	24.6	24.4	25.8	24.9	24.5
Heart volume (mL)	796*	785	794*	746	775	876*	790**	738	740	830	768	737
Never smoked (%)	18	25	19	28	31	0*	25	31	42	42	42	30
During follow-up	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Diabetes	29	38	31*	17	23	44*	27	17	21	42*	28	16
Ischemic heart disease	29	38	31	27	23	33	25	20	12	8	11	11
Myocardial infarction	29	25	28	21	21	22	21	17	12	8	11	9
Congestive heart failure	36**	38	36**	14	18	11	17	10	17	17	17*	5

* $p<0.05$, ** $p<0.01$, versus no bundle-branch block (No BBB)

Vectorcardiographic changes during acute myocardial infarction in patients with bundle-branch block (*Paper II*)

Right bundle-branch block

For patients with right bundle-branch block, both the initial ST-VM, the maximum ST-VM during the first 4 hours (Figure 12), and the QRS-vd at 12 hours (Figure 13), were significantly higher in patients with, as compared to patients without, acute myocardial infarction.

Figure 12. Boxplot of ST-VM maximum during the first four hours, for patients with right bundle-branch block. Showing the difference in distribution between patients with and without acute myocardial infarction ($p<0.01$).

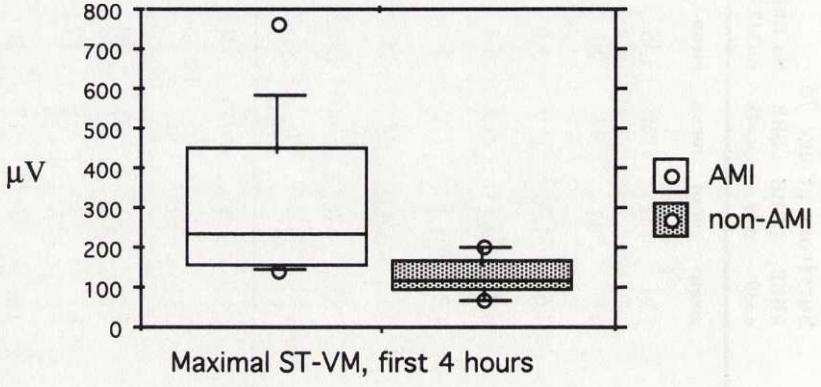
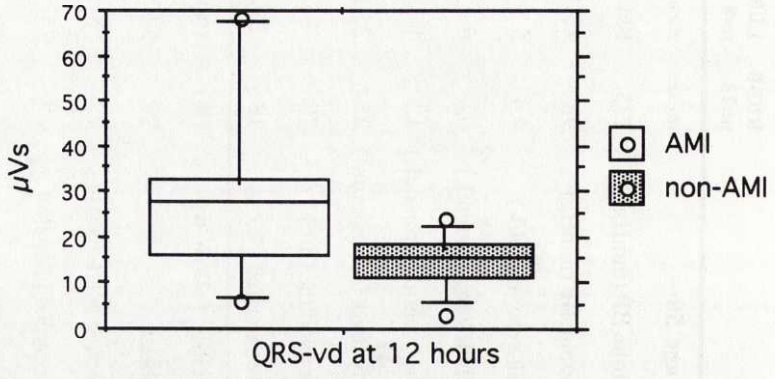
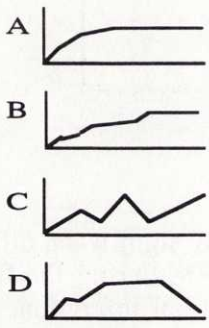


Figure 13. Boxplot of QRS-vd at 12 hours, for patients with right bundle-branch block. Showing the difference in distribution between patients with and without acute myocardial infarction ($p<0.05$).



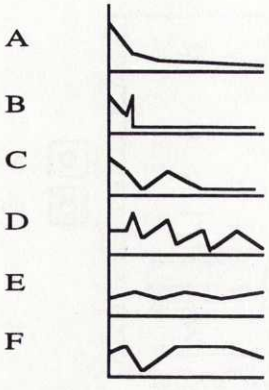
No clear trend was seen in the evolution of the QRS-vd patterns (Figure 14). In patients with ST-VM >200 μV a significant larger QRS-vd at 12 hours compared to patients with ST-VM ≤200 μV (28±13 μVs versus 11±6 μVs; $p<0.01$) was observed. The ST-VM patterns were significantly different for patients, with as compared to without, acute myocardial infarction (Figure 15).

Figure 14. Results of comparing the QRS-vd trend patterns in patients with right bundle-branch block, with versus without acute myocardial infarction (p=ns).



	acute myocardial infarction	
	yes	no
A	3	1
B	2	2
C	0	0
D	6	9

Figure 15. Results of comparing the ST-VM trend patterns in patients with right bundle-branch block, with versus without acute myocardial infarction ($p<0.01$).



	acute myocardial infarction	
	yes	no
A	2	0
B	1	0
C	3	0
D	3	2
E	0	8
F	2	2

For patients with right bundle-branch block the best single VCG criteria for diagnosing an acute myocardial infarction was found to be a maximal ST-VM >200 μV during the first four hours of recording, giving the possibility to identify 64% of all acute myocardial infarctions with a specificity of 100% (Figure 16).

Figure 16. Best retrospective criteria versus clinical diagnosis, in patients with right bundle-branch block.

ST-VM >200 uV	acute myocardial infarction: yes	acute myocardial infarction: no
yes	7	0
no	4	12

Left bundle-branch block

For patients with left bundle-branch block, no significant differences were seen in the initial ST-VM or the maximal ST-VM during the first 4 hours in patients with compared to without acute myocardial infarction. In contrast to patients with right bundle-branch block a trend for higher ST-VM was seen in patients with left bundle-branch block not having acute myocardial infarction (Figure 17). No clear trend was seen in the evolution of ST-VM patterns (Figure 18).

Figure 17. Boxplot of initial ST-VM and maximum ST-VM, during first four hours, in patients with left bundle-branch block. Showing distribution of patients with versus without acute myocardial infarction (p=ns).

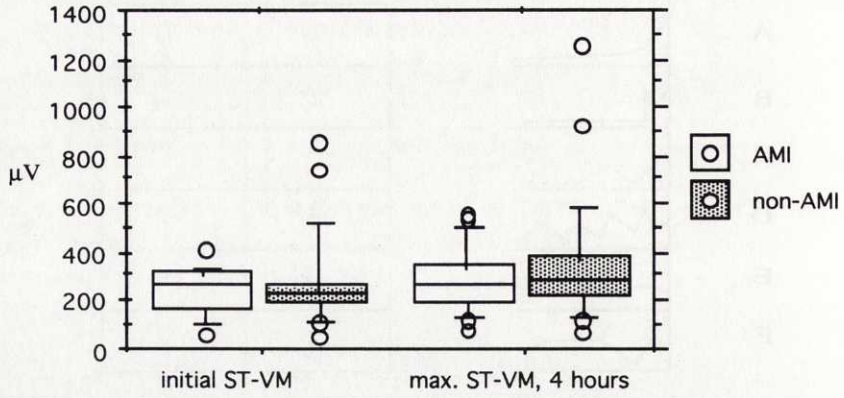
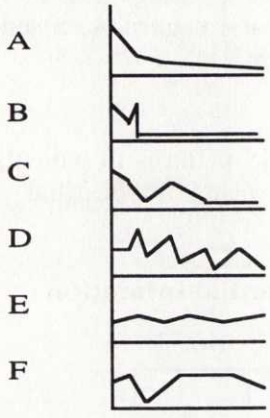


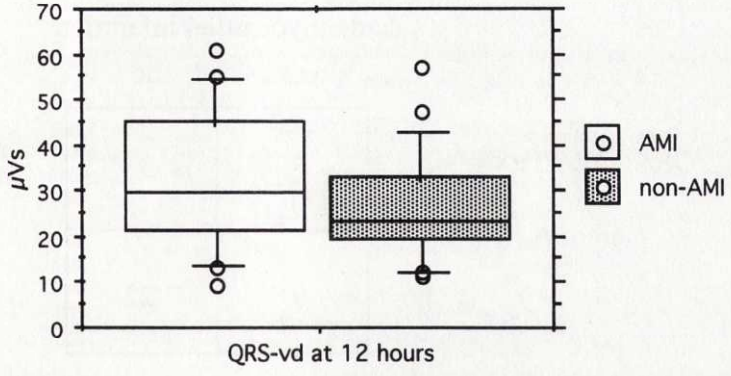
Figure 18. Results of comparing the ST-VM trend patterns in patients with left bundle-branch block, with versus without acute myocardial infarction (p=ns).



	acute myocardial infarction	
	yes	no
A	0	1
B	0	2
C	4	0
D	4	9
E	3	8
F	6	5

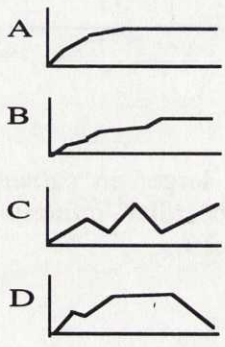
As for right bundle-branch block QRS-vd was larger in patients with left bundle-branch block developing an acute myocardial infarction, but the difference was not statistically significant (Figure 19).

Figure 19. Boxplots of QRS-vd at 12 hours in patients with left bundle-branch block. Comparing patients with versus without acute myocardial infarction (p=ns).



When analyzed according to the QRS-vd pattern, patients with left bundle-branch block more often developed pattern A, indicating acute myocardial infarction, while pattern D was mainly seen in patients without acute myocardial infarction (Figure 20). QRS-vd pattern A is characterized by an initial steady inclining trend that reaches a steady plateau, for all patients developing pattern A (13 of whom 10 had an acute myocardial infarction) this plateau was established within 4 hours of recording (range 110-233 minutes). By using the combination of QRS-vd >20 μVs and pattern A, a sensitivity of 47% and specificity of 88% was achieved (Figure 21).

Figure 20. Results of comparing QRS-vd trend patterns in patients with left bundle-branch block, with versus without acute myocardial infarction ($p<0.01$).



	acute myocardial infarction: yes	acute myocardial infarction: no
A	10	3
B	2	4
C	2	2
D	3	16

Figure 21. Best retrospective criteria versus clinical diagnosis in patients with left bundle-branch block.

		acute myocardial infarction: yes	acute myocardial infarction: no
QRS-vd >20 uVs + pattern A	yes	8	3
	no	9	22

Prospective testing of standard 12-lead ECG for diagnosing acute myocardial infarction

Right bundle-branch block (Paper III)
By using the same standard 12-lead ECG criteria, on the admission ECG, for acute myocardial infarction as for narrow QRS complex and adding ST depression ≥2 millimeters in any precordial lead (criteria 3-5 in Table III), a diagnostic accuracy of 74% was achieved.

Table III. Standard 12-lead ECG criteria versus clinical diagnosis for acute myocardial infarction in patients with right bundle-branch block.

	ECG on admission					ECG after 12-24 hours				
ECG criteria	AMI n=11	non-AMI n=12	sens.	spec.	p	AMI n=11	non-AMI n=12	sens.	spec.	p
1. Q wave >30 ms	6	7	55%	42%	ns	7	7	64%	42%	ns
2. Pathological R wave progression, precordial	3	5	27%	58%	ns	6	2	54%	83%	0.09
3. ST elevation ≥ 2mm in V1-V6	3	2	27%	83%	ns	2	2	18%	83%	ns
4. ST elevation ≥ 1mm in extremity leads	5	1	45%	92%	0.07	4	0	36%	100%	<0.05
5. ST depression ≥ 2mm in V1-V6	4	1	36%	92%	0.15	2	2	18%	83%	ns
6. Any of criteria 4-5	7	2	64%	83%	<0.05	5	2	45%	83%	ns
7. Any of criteria 3-5	8	3	73%	75%	<0.05	6	4	50%	67%	ns

AMI= acute myocardial infarction, non-AMI= no acute myocardial infarction, sens.= sensitivity, spec.= specificity. P value >0.20, unless indicated (Fischer´s exact, two tailed).

Left bundle-branch block (Paper IV)
No one of the ECG criteria tested (Table IV), on the admission ECG or the 12-24 hours ECG, differed significantly between those developing an acute myocardial infarction and those who did not. When looking at additional information given by serial comparison, the development of criteria in the 12-24 hours ECG was more common in patients not developing an acute myocardial infarction, as shown in Figure 22. Maximal ST elevation or depression tended to be more prominent in patients not having an acute myocardial infarction. Moreover, ST elevation >5 millimeters, 80 ms after the J-point in precordial leads V1-V3 was found in 58% of the patients not having

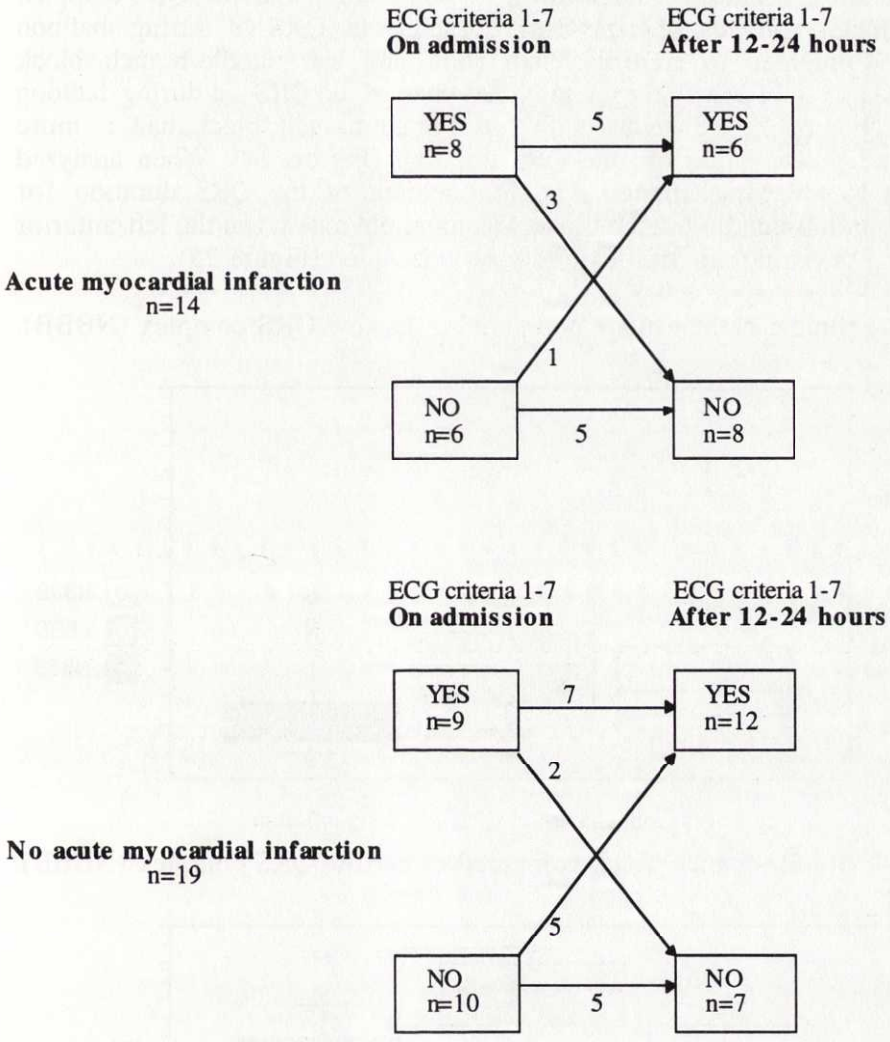
an acute myocardial infarction. In precordial leads 31 patients (94%) had their maximal ST elevation in V1-V3 and maximal ST depression was seen in V5-V6 in 23 (70%), in a total of 33 patients.

Table IV. Standard 12 lead ECG criteria versus clinical diagnosis of acute myocardial infarction in patients with left bundle-branch block.

	ECG on admission				ECG after 12-24 hours			
ECG criteria	AMI n=14	non-AMI n=19	sens.	spec.	AMI n=14	non-AMI n=19	sens.	spec.
1. ST elevation ≥ 1 mm concordant to QRS.	0	0	0%	100%	0	0	0%	100%
2. ST depression ≥ 1 mm in V1, V2 or V3.	0	1	0%	95%	0	0	0%	100%
3. ST elevation ≥ 5 mm discordant to QRS.	3	5	21%	74%	0	3	0%	84%
4. Q wave in I, aVL, or V5-V6.	1	0	7%	100%	2	0	14%	100%
5. R wave regression in V1-V4.	1	6	7%	68%	2	5	14%	74%
6. Notched upstroke of the S wave in V3-V5	4	3	29%	84%	4	3	29%	84%
7. ST segment / T wave concordant to QRS.	1	1	7%	95%	0	3	0%	84%
8. Any of criteria 1-3	3	5	21%	74%	1	3	7%	84%
9. Any of criteria 4-7	6	6	43%	68%	6	10	43%	47%
10. Any of criteria 1-7	8	9	57%	53%	6	12	43%	37%

AMI= acute myocardial infarction, non-AMI= no acute myocardial infarction, sens.= sensitivity, spec.= specificity, notched= any reversal of direction with subsequent return to the original direction.
Criteria 1-3 refers to the work by Sgarbossa (127) and criteria 4-7 refers to the MILIS study (125). Criteria 1-3 are measured at the J-point.
P value= ns, for all criteria and combinations (Fischer´s exact, one-tailed).

Figure 22. Serial 12-lead ECG comparison for diagnosing acute myocardial infarction in the presence of left bundle-branch block.



ECG criteria refers to Table IV.

Detection of ischemia during coronary angioplasty in patients with bundle-branch block using continuous vectorcardiography (*Paper V*)

QRS-vector difference (QRS-vd)
Both right and left bundle-branch block as well as their narrow QRS complex controls had significant changes from baseline in QRS-vd during balloon inflation. Compared to controls, both right and left bundle-branch block patients had a significantly larger maximal change of QRS-vd during balloon inflation (Figure 23). Patients with left bundle-branch block had a more pronounced prolongation of the QRS duration (Figure 24). When analyzed according to the vessel dilated this prolongation of the QRS duration for patients with left bundle-branch block was more obvious when the left anterior descending or the left circumflex artery was occluded (Figure 25).

Figure 23. Bundle-branch block compared to narrow QRS complex (NBBB).

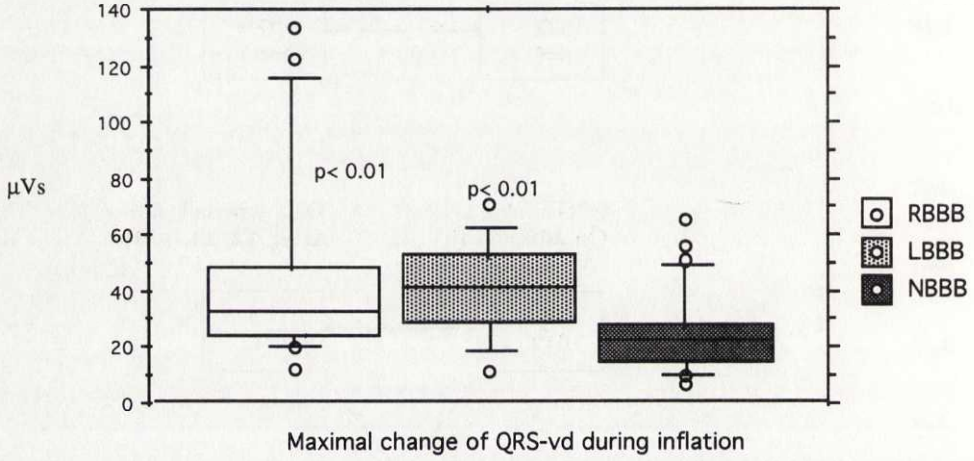


Figure 24. Bundle-branch block compared to narrow QRS complex (NBBB).

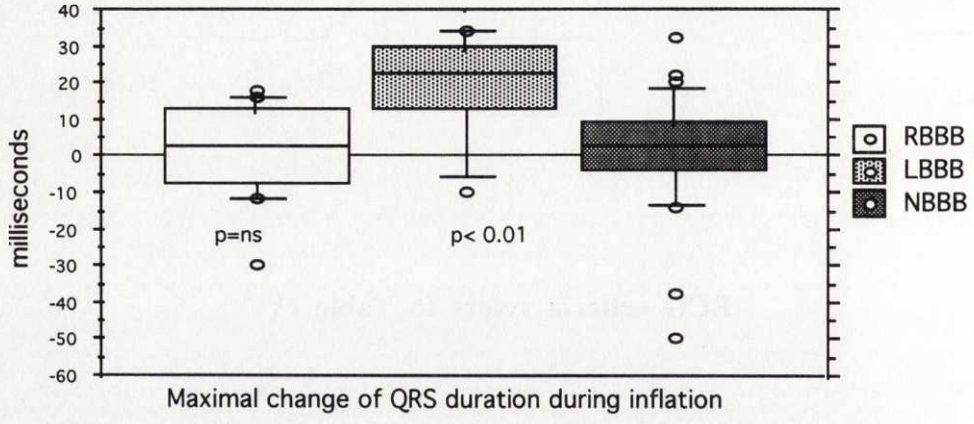
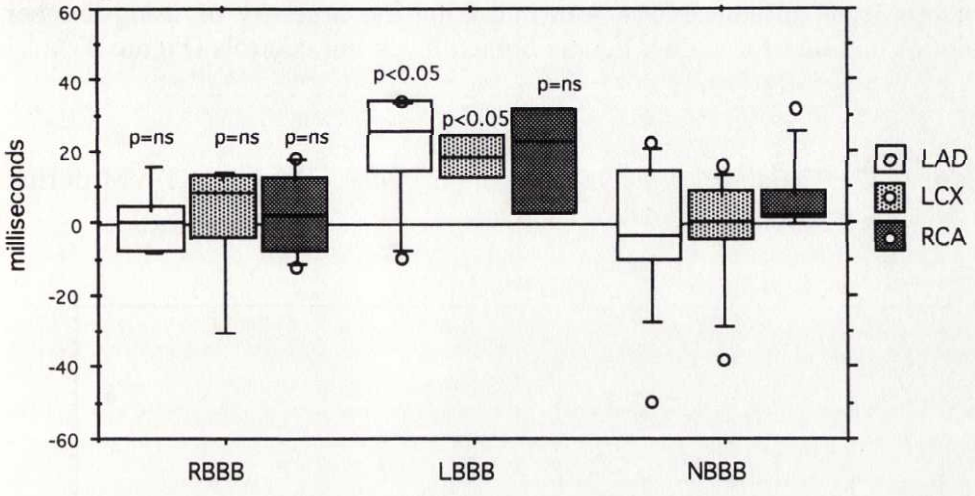


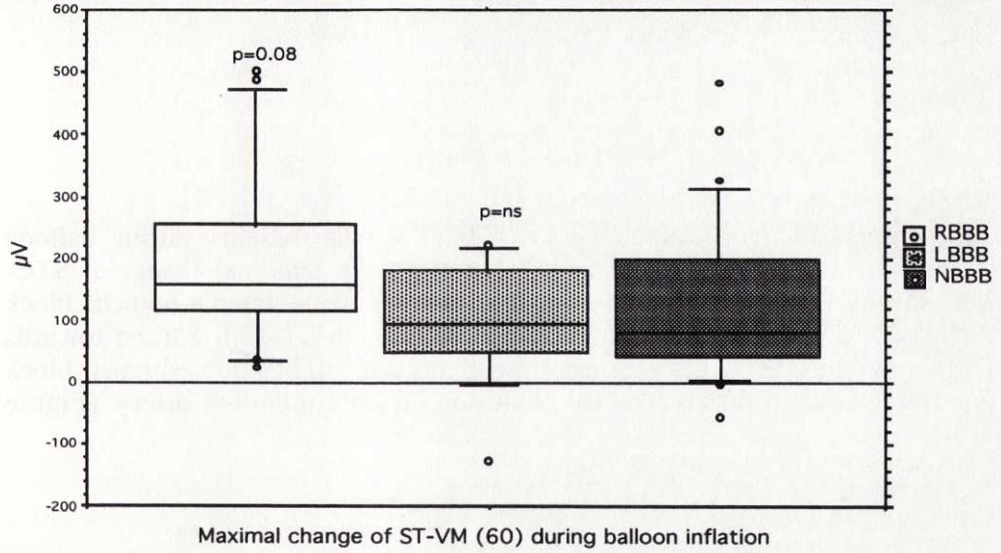
Figure 25. Bundle-branch block compared to narrow QRS complex (NBBB) according to vessel dilated.



ST-vector magnitude (ST-VM)

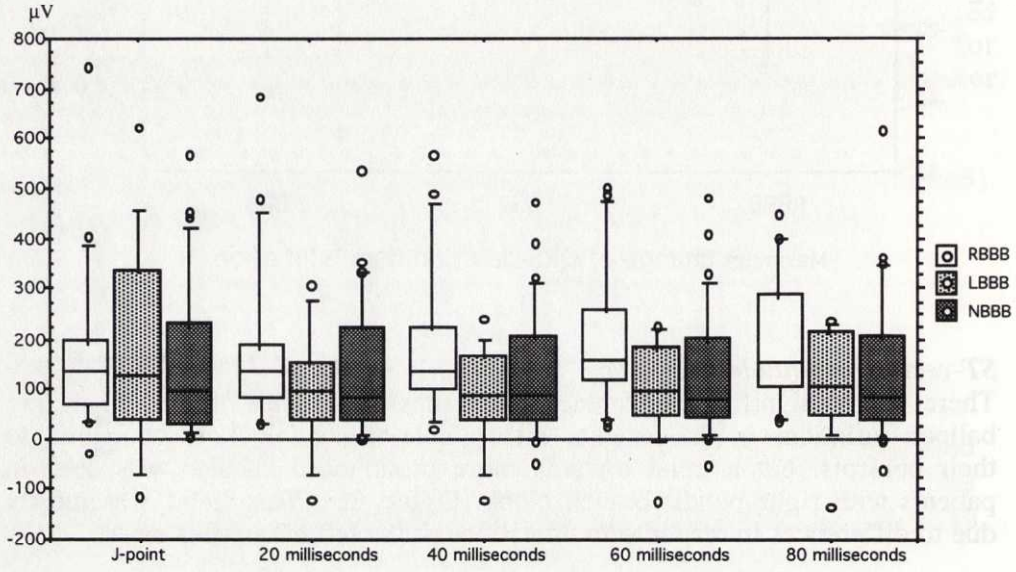
There was no significant difference in the maximal change of ST-VM during balloon inflations in the patients with bundle-branch block as compared to their controls, but a trend towards more pronounced changes was seen in patients with right bundle-branch block (Figure 26). This trend was mostly due to differences in response to dilatations of the left circumflex artery.

Figure 26. Bundle-branch block compared to narrow QRS complex (NBBB).



All measurements of ST-VM and STC-VM were done 60 ms after the J-point. When analyzed separately at the J-point, 20, 40, 60, or 80 ms after the J-point, no significant difference was seen indicating the necessity of using another point of measure for neither bundle-branch block nor controls (Figure 27).

Figure 27. Variation of the value of the maximal change of ST-VM during occlusion, depending on point of measure.



ST change-vector magnitude (STC-VM)
All patients had significant changes of STC-VM from baseline during balloon inflation. There were no significant difference in the maximal change of STC-VM during balloon inflations in the patients with bundle-branch block compared to their controls (Figure 28) but as seen in ST-VM, a trend towards more pronounced changes was seen in patients with right bundle-branch block due to significant differences for occlusion of left circumflex artery (Figure 29).

Figure 28. Maximal change of STC-VM during occlusion in patients with bundle-branch block versus narrow QRS complex (NBBB).

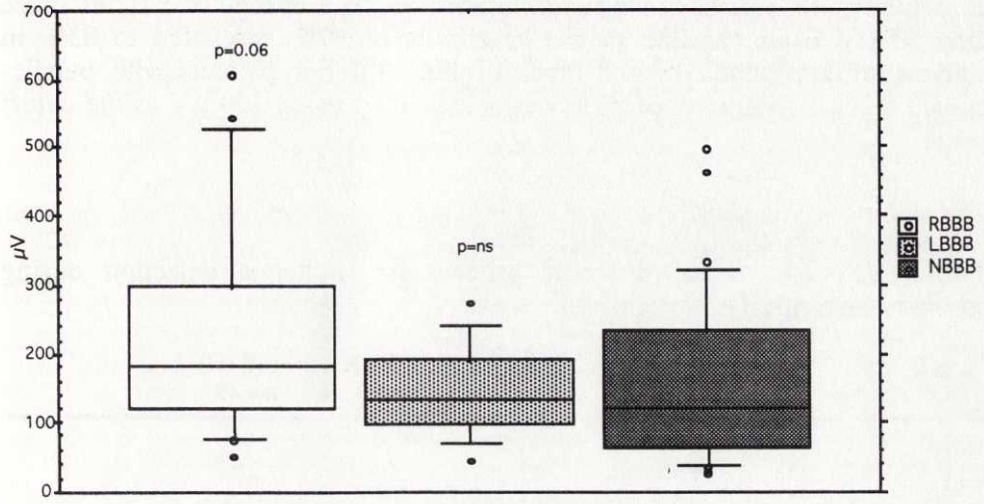
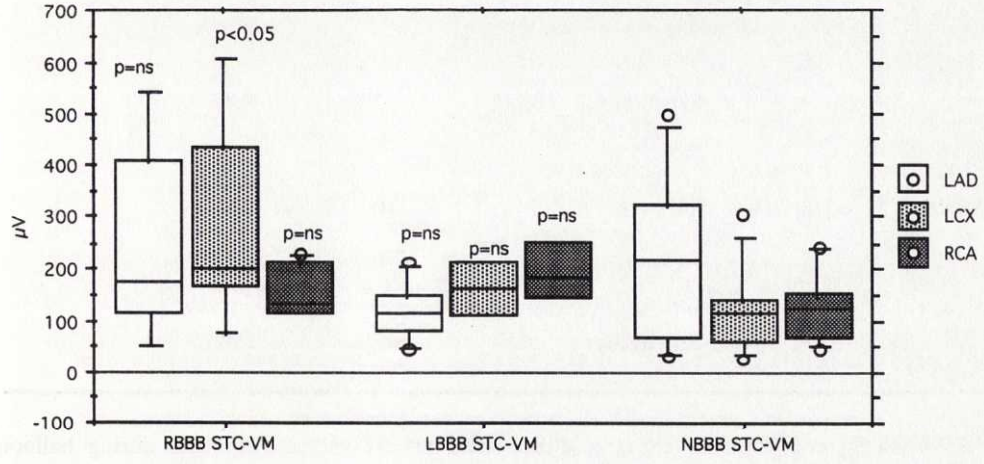


Figure 29. Maximal change of STC-VM during occlusion in patients with bundle-branch block versus narrow QRS complex (NBBB), according to vessel occluded.



Sensitivity for ischemia detection
When using earlier suggested criteria (160) for ischemia detection in patients with narrow QRS complex, STC-VM shows a better sensitivity than ST-VM in all patients. For patients with bundle-branch block, a change of STC of more than 50 μV from baseline gave a sensitivity of 97% compared to 83% in patients without bundle-branch block (Table V). For patients with bundle-branch block a sensitivity of 83% was achieved by using 100 μV as the cutoff value.

Table V. Outcome of different criteria for ischemia detection during coronary angioplasty.

		RBBB n=16	LBBB n=13	NBBB n=29
ΔST-VM >50 μV:	YES (n)	13	10	20
	NO (n)	3	3	9
	Sensitivity:	81%	77%	69%
ΔSTC-VM >50 μV:	YES (n)	16	12	24
	NO (n)	0	1	5
	Sensitivity:	100%	92%	83%
ΔSTC-VM >100 μV:	YES (n)	14	10	17
	NO (n)	2	3	12
	Sensitivity:	88%	77%	59%

ΔST-VM= ST-vector magnitude at baseline - maximal ST-vector magnitude during balloon inflation.
ΔSTC-VM= ST change vector magnitude at baseline - maximal ST change vector magnitude during balloon inflation.

DISCUSSION

Epidemiological findings in a general male population

Cumulative incidence

The results explain the wide prevalence range noted in earlier studies (26, 29, 35-38). By showing that the prevalence of bundle-branch block is highly age dependent, going from uncommon (1.2%) at the age of 50 to common (17%) at the age of 80, in the same population. Moreover, that bundle-branch blocks found in an elderly population are to the vast majority acquired. In the present study 86% were known to be acquired after the age of 50. The cumulative incidence of 18.1% shows that almost every fifth man will have or develop bundle-branch block if he lives to the age of 80.

Relationship with coronary heart disease

In the Framingham Heart Study (74), univariate analysis showed an increased risk of subsequent development of coronary heart disease or congestive heart failure in patients developing bundle-branch block. When adjusted for age, this difference in risk was not significant. Froelicher et al. (20) examined 75 asymptomatic male aircrew members with bundle-branch block with coronary angiography. They found significant stenoses in 16 (22%) of the men but no causal correlation to the length of the left main coronary artery and numbers of septal perforators in left bundle-branch block, as stated earlier in a study by Herberts (57). Patients with chest pain and right bundle-branch block were angiographically studied by Haft, and no difference in severity or extension in coronary artery disease was seen as compared to controls (53). From the Coronary Artery Surgery Study (99), 522 patients with bundle-branch block were identified. No particular location of coronary stenosis or left ventricular wall motion abnormalities predominated, indicating that the bundle-branch block was not the result of infarction of the proximal conduction system.

In the present study, when looking at risk factors for coronary heart disease at age 50, there was no difference between those who developed bundle-branch block versus those who did not. There was an exception for diabetes mellitus, which was more common in men with bundle-branch block. The risk of having or developing ischemic heart disease/myocardial infarction in the future was not higher in the bundle-branch block population. In the study population, coronary heart disease did not seem to play any major role in the development of bundle-branch block. Instead the results support the theory that bundle-branch block is a progressive degenerative disease, not only affecting the conduction system but also the myocardium itself. This is shown by a larger heart volume at age 50 in those who developed bundle-branch block at follow-up and a significantly higher incidence of congestive heart failure during follow-up. The larger heart volume cannot be explained as a result of the conduction defect since it was not present at the time of the X-ray examinations in the majority of cases (87%). Also, it seems very unlikely to be the result of extensive subclinical ischemic heart disease not shown in

difference in coronary risk factors or incidence in clinical ischemic heart disease during 30 years of follow-up.

Bundle-branch block as a marker of poor prognosis

In the present study, no statistically significant increase in mortality or death due to cardiovascular disease was seen in men with bundle-branch block at follow-up.

The marked increase in mortality in patients with bundle-branch block is only seen in combination with concomitant cardiovascular disease, in particular myocardial infarction (80, 89, 90, 99, 103, 171, 172). In bundle-branch block, the depolarization phase is by definition prolonged. Furthermore, the prolongation of the vulnerable repolarization phase, in combination with an increased number of premature ventricular beats (secondary to ischemic heart disease), would expose the patient to an increased risk of sudden ventricular tachyarrhythmias.

This theory is supported by electrophysiological studies of patients with bifascicular block where sustained monomorphic ventricular tachycardia was induced exclusively in patients with a previous myocardial infarction (173). Furthermore, several studies of patients with bundle-branch block have observed an increased risk of sudden death, not due to bradyarrhythmias but to tachyarrhythmias (14, 110-112).

Another explanation of the higher mortality seen from acute myocardial infarction could be that as a degenerative cardiomyopathy the patient is less able to compensate for a sudden loss of functional myocardium during the course of an acute myocardial infarction.

The impression is that bundle-branch block, in a healthy individual, only has marginal effect on duration of life. But in patients with the combination of bundle-branch block and ischemic heart disease the risk of death is substantially increased as compared to patients with ischemic heart disease but without bundle-branch block.

Limitations of the epidemiological study

The present study only looked at ECG recordings on four occasions during a follow-up period of 30 years. In men regarded as not having bundle-branch block who died, we do not know if they had developed a bundle-branch block before death. If that number is substantial, our results may underestimate the cumulative incidence and mortality in men with bundle-branch block.

Electrocardiographic diagnosis of acute myocardial infarction in patients with right bundle-branch block

The development of acute myocardial infarction is a dynamic process which is often not revealed by a single electrocardiographic recording (174-176). The electrocardiographic changes in acute myocardial infarction evolve very differently over time depending on whether you are looking at the QRS complex, the ST segment or the T wave. In addition there are large interindividual variations (177, 178).

In the present study of 23 patients with right bundle-branch block, 12-lead ECG on admission showed a similar performance for diagnosing acute myocardial infarction in patients with right bundle-branch block as has previously been shown for patients with narrow QRS complex (179, 180). A diagnostic accuracy of 74% was observed.

By monitoring patients for four hours with continuous VCG, a higher diagnostic accuracy was achieved (83%) by using ST-vector magnitude >200 μV, mainly by improved specificity (100%). An additional two patients with acute myocardial infarction were detected by the VCG criteria chosen, while three patients with acute myocardial infarction according to 12-lead ECG criteria did not fulfill the VCG criteria chosen.

With the combination of the 12-lead ECG criteria on admission and an ST-vector magnitude of >200 μV during the first four hours of monitoring an improved sensitivity of 91% could be achieved while maintaining an acceptable specificity of 75% (Figure 30).

Figure 30. Best combination of 12-lead ECG and vectorcardiographic criteria.

		Acute myocardial infarction	
		YES	NO
ST-VM >200uV and/or ECG criteria	YES	10	3
	NO	1	9

Sensitivity= 91%, specificity= 75%, positive predictive value= 71%, negative predictive value= 90%, diagnostic accuracy= 83%.

Fischer´s exact ; $p < 0.01$.

The changes of both the QRS-vd and ST-VM seen in patients with right bundle-branch block are more similar than different to the changes seen in patients with narrow QRS complex (139). That is, an increasing QRS-vd over time reaching a plateau and a high, or briefly increasing, ST-VM followed by a declination to a lower plateau.
The mortality in this population was high, even when the advanced age of the population was considered. This is in line with previous reports where it has been shown that in patients with chronic coronary artery disease, right bundle-branch block is an independent predictor of mortality (99, 102). The present study is too small for any conclusions to be drawn, or recommendations to be made, but it supports the hypothesis that, in patients with right bundle-branch block ST segment changes occur in the same way as for patients with narrow QRS complex. By adding four hours of continuous VCG monitoring it was possible to identify patients with acute myocardial infarction with an improved sensitivity and a high diagnostic accuracy. This underlines the importance of the additional information obtained by continuous, on-line ST monitoring.

Today, ECG criteria play a central role for selecting patients with chest pain to different treatments, notably thrombolytic treatment. For patients with chronic right bundle-branch block there are no commonly accepted guidelines. In a recently performed study on thrombolytic treatment (GUSTO III) (181) the mere presence of right (or left) bundle-branch block implied eligibility for inclusion in the study. If you would extrapolate the GUSTO III inclusion criteria into clinic practice and treat all patients with >30 minutes of chest pain and right bundle-branch block with thrombolytics, you would probably expose many patients not having an acute myocardial infarction for the risk of adverse effects of the treatment. As shown in *Paper I*, bundle-branch block is common in the elderly, who also have a higher risk of experience adverse effects of thrombolytics (182). On the other hand, too much hesitation when right bundle-branch block is present, will result in undertreatment. If well-defined ECG and VCG criteria can be validated, the risk of over- and underuse of thrombolytics will diminish, thereby further reducing the mortality in this high-risk population.

Electrocardiographic diagnosis of acute myocardial infarction in patients with left bundle-branch block

The ST segment and T wave abnormalities encountered with left bundle-branch block are probably the most frequently misinterpreted pseudoinfarction pattern in practice today (183, 184). Diagnosing acute myocardial infarction with a single standard ECG in patients with left bundle branch block is difficult. Several studies have indicated that changes in the QRS complex and in the ST-T segment on the standard ECG have a high specificity but a low sensitivity for detecting a myocardial infarction (113, 120, 121, 125). Over 55 different ECG criteria have been proposed as predictors of myocardial infarction over the years but only a few have been shown to be useful when

tested prospectively, all with very low sensitivity for diagnosing myocardial infarction (125, 131).
In our study of 33 patients of whom 14 had a clinical diagnosis of acute myocardial infarction, the seven most promising suggested ECG criteria were not helpful due to a diagnostic accuracy much too low for clinical use.
The recently suggested criteria by Sgarbossa et al. (127) have gained a wide acceptance (185). Two of the three criteria described by Sgarbossa et al. were not present in any patient and the third, a prominent ST elevation discordant to the QRS complex in V1-V3 is common in patients with left bundle branch block, with or without acute myocardial infarction. Moreover, the ECG criteria tested in *Paper IV* could be transient (5 patients) or develop (6 patients) both in patients with and without an acute myocardial infarction. The conclusion must be that recording of one or two standard ECGs is insufficient to correctly diagnose acute myocardial infarction in patients with left bundle branch block. This further underlines the importance of the additive information achieved by continuously monitoring the QRS complex and ST levels.
No single vectorcardiographic parameter was found to be of significant diagnostic value in this study. However, we found that using QRS-vector difference trend patterns made it possible to significantly separate those who developed an acute myocardial infarction from those who did not. Since the QRS-vector difference measures all changes in relation to the initial QRS complex, the complexity of the electrocardiographic changes in acute myocardial infarction for patients with left bundle branch block, may be less difficult to detect, understand, and illustrate, using this technique. The study in *Paper II* focused on a first description on cVCG in acute myocardial infarction. Using 12 hours of recording for pattern recognition is to long to be of any significant clinical value, since by then too much time has passed for aggressive revascularisation strategies. However, it shows that changes in the QRS complex develop early in the phase of an acute myocardial infarction. In patients with pattern A the characteristic plateau was reached in the range of 110-233 minutes. Our study suggests that vectorcardiography may be of use in the diagnosis of acute myocardial infarction in patients with chronic left bundle-branch block, but this suggestion needs to be confirmed in a larger study.

One explanation for the poor performance of electrocardiographic as well as vectorcardiographic criteria may be that they are transient in the early course of acute myocardial infarction. No upper time limit from onset of symptoms to start of vectorcardiographic recording and 12-lead ECG on admission was used in the present study. Thus, since electrical and enzymatic biological lag time are different, we may in some patients have started monitoring after most of the electrocardiographic /vectorcardiographic changes had already taken place. An alternative reason may be the limited number of patients in this study. However, the study group is similar in size to the 45 patients in the validation sample in Sgarbossas work (127), and the 10 patients with left bundle

branch block and acute myocardial infarction in the MILIS study (125), as well as the 36 patients with persistent bundle branch block (right and left were not described separately) and acute myocardial infarction in the published work by Newby et al in Circulation (102).

If the VCG is to play a significant part in the early detection of acute myocardial infarction in patients with left bundle-branch block, it is likely to be in regard to its superiority over the electrocardiogram in demonstrating QRS abnormalities (186-188). The problem with studying the QRS complex is that changes occur not only due to ischemia but also possibly due to changes of intra cardiac blood volume (189), ventricular size and position (190), QRS-axis (191) and intramyocardial conduction (192). By studying the trend pattern of QRS-vd it may be possible to partly overcome these difficulties. In order to detect acute myocardial infarction as early as possible, the QRS-vd may need refinement by combining the trend with QRS duration (*Paper V)* and/or the angle between the QRS vector and ST-T vector (137).

Continuous vectorcardiographic monitoring of transient ischemia in patients with bundle-branch block

Using coronary angioplasty as an ischemia model has its limitations. Several steps in the procedure have the possibility of affecting coronary blood flow therefore inducing ischemia. Some of these limitations include engaging the coronary ostia with a guide, injecting contrast, passing tight stenosis with the wire, and positioning the uninflated balloon. In order to overcome this only the maximal change from baseline during balloon inflation was studied.

To describe the area of ischemia with coronary angiography as golden standard has several pitfalls. The individual anatomy of which vessel/vessels that are dominant are hard to describe for groups due to a wide range of variations. Moreover, a brisk epicardial flow does not necessarily mean perfusion on tissue level (193) and total occlusions are not equal to total necrotic myocardium, due to the possibility of collateralization. In *Paper V* patients with bundle-branch block were older and had more extensive coronary heart disease than their narrow QRS-complex controls. In what way that difference will affect our results is hard to analyze; will the area of ischemia from the balloon occlusion be generally larger or smaller if you have more extensive coronary heart disease?

All our patients were scheduled to undergo angioplasty on clinical indications where the stenosis was judged to be the culprit lesion for an ischemic area.

In *Paper V,* both right and left bundle-branch block as well as their narrow QRS-complex controls had significant changes from baseline in QRS-vd, ST-VM and STC-VM, during balloon occlusion of a coronary artery. Maximal simultaneous changes of the three parameters during balloon inflations were quite similar whether bundle-branch block was present or not, except for a significantly larger change in QRS-vd and a trend towards larger change in ST-VM and STC-VM in patients with bundle-branch block. In patients with left bundle-branch block the QRS-vd change was combined with a significant

prolongation of the QRS duration. Since the algorithm for calculating QRS-vd only considers the time period set by the reference complex, prolongation of the QRS duration is a separate finding. Alterations in the QRS complex have mostly been associated with myocardial necrosis. However, changes in the QRS complex (in patients with narrow QRS complex) during acute transient coronary occlusions have been reported using different techniques (194-198) probably explained by the appearance of a "peri-ischemic block" causing a delayed and unopposed ventricular activation of the ischemic area, causing a change in direction as well as an increase in magnitude of the mean QRS vector.

The results confirm that changes in the QRS complex do occur as a response to temporary occlusion of a coronary artery, in patients with as well as without bundle-branch block measured as QRS-vd. The study in *Paper V* is the first describing changes of the QRS complex in patients with bundle-branch block during transient ischemia. QRS-vd has not previously been paid much attention in monitoring patients with unstable angina due to a wide intrapatient variation of mostly QRS amplitude, secondary to, e.g., position in bed, changes of chamber size, heart rate, and change in electrode position (190, 199-201). Whether the combination of change of QRS-vd together with prolongation of the QRS duration in patients with left bundle-branch block will be more specific and useful in monitoring ischemia remains to be studied.
In *Paper II,* diagnosing acute myocardial infarction using cVCG in patients with bundle branch block, analysis of ST-VM was only diagnostic in right bundle branch block. In patients with left bundle-branch block there was no significant difference between those having an acute myocardial infarction or not. Since ST-VM does significantly increase during balloon occlusion even in patients with left bundle-branch block, as shown in this study, the message seems contradictory. One explanation could be that increases in ST-VM occur fast and are transient even when there is a longer (hours to permanent) coronary occlusion and would have been missed in the monitoring of acute myocardial infarction due to patient- and hospital delay. If that is the case, ST-VM monitoring of patients with left bundle-branch block and unstable coronary syndrome can still be used.

In an animal study STC-VM had a higher sensitivity than ST-VM in detecting small ischemic territories (166). In humans, Jenssen et al. found similar results during angioplasty (160). The rationale behind this is that predominantly directional changes of the ST vector may not be displayed in an ST-VM trend curve.
The present study shows the same i.e., that STC-VM has a higher sensitivity than ST-VM in patients with narrow QRS complex. For patients with bundle-branch block STC-VM had at least the same sensitivity for detecting ischemia as in patients with narrow QRS complex. Since we did not have simultaneous analysis of an independent variable such as lactate balance, we have not been able to verify the specificity of ischemia during the balloon inflation. Though

we do not know the specificity of STC-VM in detecting myocardial ischemia, one may speculate in using a higher cut off for patients with bundle branch block. By using a change of STC-VM >100 μV as criteria for ischemia in patients with bundle-branch block, we would in our patient group, obtain the same sensitivity for patients with bundle branch block (83%) as the criteria STC-VM > 50μV (suggested by Jenssen et al.(160)) would obtain for patients with narrow QRS complex.

Clinical implications

Presently it is difficult to evaluate a 12-lead ECG in a patient with atypical chest pain after a recently performed angioplasty, when bundle-branch block is present. Our findings indicate that on-line cVCG is useful in the monitoring of acute myocardial ischemia even in patients with bundle-branch block during and after angioplasty. Using continuous, on-line VCG monitoring a fast recognition of early reocclusions will be possible.

Whether the number or magnitude of ST-VM and/or STC-VM episodes carry the same prognostic information in patients with unstable angina and bundle branch block as has been reported for patients with narrow QRS complex (155, 156), remains to be studied.

The present study indicates that an STC-VM change from baseline >100 μV could be used in patients with bundle-branch block to define significant episodes of ischemia, especially if combined with QRS-vd increase and in patients with left bundle-branch block, prolongation of the QRS duration.

SUMMARY AND CONCLUSION

- Bundle-branch block was found to be common in elderly men and increased with age.

*

- The majority of bundle-branch blocks are acquired after the age of 50.

*

- No correlation between the development of bundle-branch block and risk factors for ischemic heart disease at age 50, hospitalization due to ischemic heart disease or cardiovascular death during follow-up, was found.

*

- The results support the theory that bundle-branch block is mainly a marker of a progressive degenerative disease which also affects the myocardium.

*

- The presence of bundle-branch block in a general male population has only marginal effect on survival.

*

- In both right and left bundle-branch block QRS-vd changes during acute myocardial infarction occurred in a similar manner to that in patients with narrow QRS complexes.

*

- QRS-vd patterns of evolution provided additive information for diagnosing acute myocardial infarction in patients with left bundle branch block.

*

- In right bundle-branch block ST-VM changes during acute myocardial infarction occurred in a similar manner to that in patients with narrow QRS complexes.

- By using ST-VM maximum >200 μV, during the first 4 hours of monitoring, a diagnostic accuracy of 83% was achieved for diagnosing acute myocardial infarction in patients with right bundle-branch block.

*

- In left bundle-branch block no significant difference of ST-VM in patients with or without acute myocardial infarction was found.

*

- Previously proposed standard ECG criteria were clinically useful in patients with right bundle-branch block, but not in patients with left bundle-branch block.

*

- Detection of ischemia during angioplasty is feasible in patients with bundle-branch block.

*

- STC-VM is the parameter with best sensitivity for detecting occlusion of a coronary artery in patients with bundle-branch block as well as in patients with narrow QRS complex. A change of STC-VM of >100 μV is suggested to be used in patients with bundle-branch block as indicating a transient coronary occlusion.

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