Long-Term Prognosis of Adult Patients With Isolated Congenital Left Ventricular Aneurysm or Diverticulum and Abnormal Electrocardiogram Patterns
Marc-Alexander Ohlow, MD; Bernward Lauer, PhD; Ulrich Lotze, MD; Michele Brunelli, MD; J. Christoph Geller, PhD

Background: Congenital left ventricular aneurysm (LVA) and diverticulum (LVD) are rare cardiac anomalies frequently associated with electrocardiogram (ECG) abnormalities. The aim of this study was to evaluate the long-term prognosis in such patients.

Methods and Results: A total of 108 patients with LVA or LVD having ECG-abnormalities were assessed. The patients were classified into 2 groups according to ECG abnormalities: a distinct ECG group (8 ECG patterns known to be frequently associated with LVA/LVD); and a control group (all other ECG abnormalities). The primary endpoint was a composite of cardiac death, rhythm disturbances, syncope, embolic events, and hospitalization for cardiovascular events. Mean patient age was 64±10 years; 45 (42%) were male; median follow-up (FU) was 50 months. The primary endpoint occurred in 12/27 patients from the distinct ECG group and in 15/81 patients in the control group (44% vs. 19%; P=0.01). Cardiac event rate per year (CER) was 1.8% vs. 0.8%, respectively. There were no cardiac deaths during FU. Symptoms (arrhythmia-related symptoms, syncope, and embolic events) at time of diagnosis increased the incidence of adverse events during FU (70% vs. 28%; P=0.05; CER 2.9% vs. 1.1%). Age ≥64 years, presence of LVD, gender, and location of the anomaly did not affect the incidence of adverse events.

Conclusions: The incidence of adverse events in symptomatic patients with isolated LVA or LVD and distinct abnormal ECG patterns is increased during long-term FU. None of the present patients, however, experienced cardiac death. (Circ J 2012; 76: 2465–2470)

Key Words: Aneurysm; Congenital; Diverticulum; Electrocardiogram abnormality; Left ventricle

Conventional left ventricular aneurysm (LVA) and diverticulum (LVD) are rare malformations and approximately 500 cases have been published in the literature since the first description in 1816. A recent study found a prevalence of 0.76% in adult patients undergoing coronary angiography. Although most investigators distinguish between LVA and LVD, the cause, histopathology, and clinical implications remain controversial. The advent of echocardiography and magnetic resonance imaging has led to earlier diagnosis, including prenatal detection. The published research on these anomalies consists, beside 1 large single center study, of case reports and small case series, mostly on infants and young children with large aneurysms and poor clinical outcome. High morbidity and mortality rates due to heart failure, aneurysm rupture, thromboembolism, and sudden death of unclear cause have been reported. More recent published data demonstrated a more favorable course with no cardiac mortality in adults with congenital LVA and LVD. A significant proportion of the published literature report arrhythmias in patients with these anomalies. Recently, our own group was able to demonstrate that patients with congenital LVA/LVD had a high incidence of distinctly abnormal electrocardiograms (ECGs) compared to an age- and gender-matched control group. The purpose of the present study was to evaluate the prognosis and risk factors of patients with a diagnosis of isolated congenital LVA or LVD, having ECG abnormalities.

Methods

Definition
The diagnosis of congenital LVA or LVD was established after angiographic exclusion of coronary artery disease. Clinical and ECG local or systemic inflammation, traumatic causes and car-
diomyopathies (eg, arrhythmogenic right ventricular cardio-
myopathy) were excluded.

Definition of LVA (Figure 1) included normal size and func-
tion of the left ventricle with a- or dyskinetic structures with a
wide connection to the left ventricle. In LVD (Figure 2) this
connection to the left ventricle is narrow in a structure with
normal systolic contraction.

Diagnosis
All LV angiograms were obtained with 30 ml contrast medium
at a rate of 15 ml/s in 2 angulations (left anterior oblique 60°
and right anterior oblique 30°, respectively) and all were ana-
alyzed by 2 independent reviewers for the presence of congeni-
tal LVA or congenital LVD. The diagnosis of LVA or LVD
was made only if both reviewers agreed in the diagnosis. Spe-
cial emphasis was placed on the avoidance of pitfalls such as
prominent trabecula, clefts, aberrant papillary muscles, or cat-
beter entrapment mimicking LVA or LVD.

Subjects
Between 1 January 2001 and 31 December 2003, 17,257 con-
secutive patients underwent diagnostic coronary angiography
at Zentralklinik Bad Berka, Germany. During this time, 125
patients with angiographically proven isolated congenital LVA
or LVD were identified. Finally, 108 patients with follow-up
of at least 12 months and a 12-lead ECG available were included
in this analysis. Children younger than 16 years (because they
might represent a different group of risk) and patients with
associated congenital anomalies were excluded.

ECG
Standard 12-lead ECGs were recorded at 50 mm/s with the sub-
ject in the supine position during quiet respiration.

All ECGs were evaluated according to commonly adopted
clinical criteria by 2 independent expert cardiologists. We
arbitrarily classified ECGs into 3 subgroups as suggested by
Pelliccia et al and Surawitz et al on the basis of the presence of
≥1 of the listed criteria. The subgroups were as follows.

Distinctly Abnormal ECG Distinctly abnormal ECGs were
those that were strongly suggestive of cardiovascular disease.
The criteria for such a designation included the following: (1)
striking increase in R or S wave voltage (≥35 mm) in any lead; (2)
Q waves ≥4 mm in depth and present in >2 leads; (3) repolariza-
tion pattern with inverted T wave >2 mm in ≥2 contiguous leads; (4) left bundle branch block; (5) marked left (<−30°) or right (>110°) QRS axis deviation; and (6) Wolff-
Parkinson-White or Brugada pattern, and ε-wave.

Mildly Abnormal ECG Mildly abnormal ECGs were those
compatible with the presence of cardiovascular disease. The
criteria for such a designation included the following: (1) in-
creased R or S wave voltage (30–34 mm); (2) Q waves 2–3 mm
in depth and present in ≥2 leads; (3) repolarization patterns with
either flat, minimally inverted, or particularly tall (ie, ≥15 mm)
T waves in ≥2 leads; (4) abnormal R progression in the ante-
rior precordial leads; (5) right bundle branch block (RBBB pat-
tern, QRS ≥120 ms in V1 and V2); (6) right atrial enlargement
(peaked P waves ≥2.5 mm in leads II, III, or V1); (7) left atrial
enlargement (prolonged positive P wave in lead II and/or deep
prolonged negative P wave in V1); and (8) short PR interval
(≤120 ms), atrial fibrillation.

Normal ECG or ECG With Minor Alterations This subgroup

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**Figure 1.** Examples of congenital left ventricular aneurysms (LVA; white arrows). (A) Apical LVA; (B, C) postero-basal LVA; (D) diaphragmal LVA.
consisted of ECGs that were completely normal and those with minor alterations, for example as reported in trained athletes. These minor alterations included the following: (1) increased PR interval duration (>0.20 s); (2) mild increase in R or S wave voltage (25–29 mm); (3) early repolarization (ST-elevation ≥2 mm in ≥2 contiguous leads); (4) incomplete right bundle branch block (RSR pattern in V1 and V2 of <120 ms in duration); (5) sinus bradycardia (<60 beats/min).

In a recently published paper our group was able to demonstrate that several ECG abnormalities were more frequently encountered in patients diagnosed with LVA or LVD. These specific ECG-abnormalities included (1) repolarization pattern with inverted T wave >2 mm in ≥2 contiguous leads; (2) repolarization patterns with either flat, minimally inverted, or particularly tall (ie, >15 mm) T waves in >2 leads; (3) Q waves 2–3 mm in depth and present in >2 leads; (4) Abnormal R progression in the anterior precordial leads; (5) atrial fibrillation; (6) complete/incomplete right bundle branch block (RSR pattern, QRS >120 ms in V1 and V2); (7) early repolarization pattern (ST-elevation ≥2 mm in ≥2 contiguous leads); and (8) increased PR interval duration (>0.20 s).

Twenty-seven patients with ≥1 of the aforementioned ECG abnormalities were classified into the distinct ECG-group. The remaining 81 patients having non-specific LVA/LVD ECG alterations or normal ECG constituted the control group.

Follow-up
All clinical data were obtained by review of the patient records. At the end of the data-collecting period, all identified patients were followed up in the outpatient clinic or by a trained nurse via standardized telephone call. Follow-up was focused on survival, arrhythmic events (patients were considered to have an arrhythmic event if sudden cardiac death occurred, or if appropriate implantable cardioverter-defibrillator [ICD] shocks or sustained supraventricular/ventricular tachycardia were documented), syncope, need for pacemaker or defibrillator implantation, and recurrent hospitalizations. In the case of recurrent hospitalizations between the index coronary angiogram and the follow-up, we additionally reviewed the medical record of this particular hospital stay.

Table. Clinical Events During Follow-up

<table>
<thead>
<tr>
<th>Clinical event</th>
<th>Distinct ECG group (n=27)</th>
<th>Control group (n=81)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>12 (44.4)</td>
<td>15 (18.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Death, cardiac</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1</td>
</tr>
<tr>
<td>Rhythm disturbance, syncope</td>
<td>4 (14.8)</td>
<td>11 (14)</td>
<td>1</td>
</tr>
<tr>
<td>Embolization</td>
<td>1 (3.7)</td>
<td>2 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Cerebral</td>
<td>0 (0)</td>
<td>1 (1.2)</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral</td>
<td>1 (3.7)</td>
<td>1 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>7 (25.9)</td>
<td>9 (11.1)</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Data given as n (%).
ECG, electrocardiogram.

Figure 2. Examples of congenital left ventricular diverticula (LVD; white arrows). (A, D) Apical LVD; (B) diaphragmal LVD; (C) postero-basal LVD.
egoric variables were done using the chi-square test or Fisher exact test, as appropriate. The primary endpoint was a combination of cardiac death, rhythm disturbances, syncope, embolic events, and hospitalization due to cardiovascular events. This composite endpoint was chosen because rhythm disturbances, syncope and embolic events are the most frequent complications in patients diagnosed with LVA/LVD. Hospitalization for cardiovascular events has been used in several studies as a surrogate endpoint for cardiovascular mortality. The mean event rate per year was evaluated as the number of events occurring during the follow-up divided by the number of patients multiplied by the average duration of follow-up. The log-rank test was used to compare event rates. Clinical outcomes are presented using the Kaplan-Meier method. P<0.05 was considered to be statistically significant. PS software (Vanderbilt University Medical Center, USA) was used for statistical analyses.

Results

Subjects and ECG Abnormalities
The analysis included 108 individuals with a mean age of 64±10 years (range, 22–75) years at diagnosis. Forty-five (42%) were male. Fifty-one patients (47%) were found to have congenital LVAs, and in 57 patients (53%) congenital LVDs were diagnosed. Abnormal ECGs were identified in 61/108 patients (56%); these included 27 (25%) with specific ECG abnormalities (distinct ECG-group) and 81 (75%) with mildly/minor abnormal patterns, or completely normal ECGs (control group).

Clinical Presentation
Patients found to have LVA or LVD presented on clinical evaluation and cardiac catheterization with a wide range of symptoms. The most common complaints were syncope, palpitations and rhythm disturbances in approximately 43% (n=46) of all

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**Figure 3.** Event-free survival according to electrocardiogram (ECG) pattern.

**Figure 4.** Event-free survival according to symptoms at diagnosis.
affected patients. The second most frequent cause for invasive evaluation was chest pain in 39% of all cases (n=42). Seventeen patients (16%) had no complaints but an abnormal non-invasive stress-test, and another 3 patients (2%) had a history of embolic events (2 patients with stroke, 1 patient with peripheral embolization).

The main symptoms at the time of diagnosis in individuals with distinct ECG alterations were as follows: (1) documented arrhythmias, palpitations, and syncope in 8 patients (29.6%); (2) embolic events in 3 (11%); and (3) lack of symptoms in 16 (59.3%).

**Treatment**

Ten patients (9%), 7 of whom had previous spontaneous non-sustained VT, underwent electrophysiological testing. Another patient presented with AV-node re-entrant tachycardia, and the other 2 patients were tested for evaluation of syncope and palpitations.

On electrophysiological testing 1 patient (1%) was found to have inducible sustained monomorphic ventricular tachycardia and received an ICD. Two patients (2%) with inducible non-sustained ventricular tachycardias received amiodarone. In 1 patient (1%), programmed electrical stimulation indicated AV-node re-entrant tachycardia that could successfully be treated with radiofrequency ablation. All other 7 patients (6%) undergoing electrophysiological assessment had no inducible supraventricular or ventricular tachycardia. Another 23 patients (21%) were treated with beta-blockers, and 26 patients (24%) received oral anticoagulation: 21 of them were diagnosed with atrial fibrillation, 3 patients had embolic events without evidence of atrial fibrillation, and 2 patients because of a perceived thrombogenic potential of an aneurysm.

**Follow-up Data**

The median follow-up period for the entire study group was 50 months (range, 12–59 months; cumulative follow-up, 5,400 months). The event rate per year for the entire group was 1%. Five patients (4.6%) died from non-cardiac reasons and no cardiac deaths occurred during follow-up. The clinical events of patients with LVA and LVD during follow-up are listed in Table.

**ECG Pattern at Time of Diagnosis**

Patients from the distinct ECG group had a significantly increased incidence of the combined endpoint during follow-up compared to the control group (44.4% vs. 18.5%; log-rank, 0.01; Figure 3). The mean event rates per year were 1.8% vs. 0.8%, mainly due to an increased risk of hospitalization during follow-up (25.9% vs. 11.1%).

**Symptoms at Time of Diagnosis**

The incidence of adverse clinical events during follow-up was increased in symptomatic patients from the distinct ECG group vs. the control group (70% vs. 28%; log-rank, 0.05; Figure 4). The mean event rates per year were 2.9% and 1.1%, respectively.

**Age and Gender**

The incidence of clinical events did not differ with respect to gender, although a slightly larger proportion of male patients had events compared with female patients (46% vs. 38%; P=0.7). Older patients (≥64 years) were more likely to have events during follow-up (53% vs. 25%), although this did not reach statistical significance (P=0.1).

**Type and Location of Abnormality**

There was an excess of adverse clinical events in patients with LVD and distinct ECGs (60% vs. 33%), but this was not statistical significant (P=0.7).

We arbitrarily classified the location of the anomalies into 3 subgroups: inferior (n=10), apical (n=14) and other (n=3). Neither apical vs. non-apical location nor inferior vs. non-inferior location of the anomaly demonstrated a significant increase of the risk of adverse clinical events (57% vs. 29%; P=0.3, and 20% vs. 56%; P=0.1, respectively).

**Discussion**

The present data show that distinct ECG patterns in patients with LVA or LVD are of prognostic importance, given that the incidence of clinical events during a median follow-up period of 50 months was significantly higher in such patients compared to patients with non-specific LVA/LVD ECG changes. Another important clinical risk factor was the presence of symptoms (e.g., embolic events, rhythm disturbances, syncope) at the time of diagnosis. The event rate during follow-up in asymptomatic patients was 2.9% per year, whereas the event rate was low in asymptomatic patients (approximately 1% per year). With regard to mortality, however, follow-up had an overall benign course. During a cumulative 5,400 months of follow-up no cardiac death occurred, which is in line with the results of other studies. Mayer et al reported a series of 16 patients with follow-up over a mean of 61 months and found a mortality of 6% with no death attributable to cardiac reasons.42 Ehlers et al reported on 6 patients who remained asymptomatic during a period of follow-up ranging from 3 to 17 years.43 McMahon et al described in their series of 26 patients with LVA/LVD only 1 non-cardiac death during a mean follow-up period of 13.5 years.44 In contrast to these benign mortality data there are several reports on small cohorts of patients with LVA/LVD and much less favorable prognosis. Marijon et al demonstrated in their cohort of patients diagnosed with LVA/LVD a survival rate of only 30% after 4 years of follow-up.45 That patient group, however, consisted of neonates or young children associated with other intra- and/or extracardiac malformations, which might represent a different risk group.44 Reports of progressive enlargement or rupture of LVA/LVD exist exclusively in children,46,47,48 the present series did not include patients below the age of 16 years, and this might explain, at least in part, the low cardiac mortality.

The association between the presence of LVA/LVD and ventricular arrhythmias has been reported in several studies. The initial case reported by Maloy et al involved a 26-year-old woman with an apical LVA who had recurrent ventricular tachycardias.49 Later, Fellows et al reported a small patient series: 2 patients with aborted sudden cardiac death and 1 patient who presented with syncope and documented non-sustained ventricular tachycardias.50 Shen et al described a male patient with sustained ventricular tachycardia caused by a postero-basal LVD, which was also inducible during electrophysiological testing.51 Haegeli reported a series of 30 patients with LVA or LVD with associated ventricular tachycardia and/or syncope including 14 patients undergoing ICD implantation or ablation of the clinical ventricular arrhythmia (Haegeli LM., pers. comm., 2011). Although rhythm disturbances and syncope were the most frequent clinical problem during follow-up in the present cohort, there was only 1 ICD implantation in the series.

The proportion of abnormal ECG patterns in the present series was greater than previously reported,28 but the causal relationship between a localized aneurysm or diverticulum and ECG changes remains unclear, and the assumption of any associated cardiac remodeling process in addition to the presence of LVD remains speculative. The presence of distinct ECG patterns in patients with LVA or LVD might be a clinical sign of greater involvement of the conduction system during the development of the cardiac anomaly. The latter might lead to an increased rate of symptoms at diagnosis and an increased rate...
of adverse clinical (eg, arrhythmic) events during follow-up. Given the event rates overall, it remains difficult to recommend a suitable therapeutic approach for patients with LVA or LVD.

The risk for adverse events in the present asymptomatic patients with distinct ECG abnormalities was 1.8% per year and that for symptomatic patients with distinct ECG abnormalities was 2.9% per year. This will lead over a period of 16 years (=mean life expectancy of the present patients) to a potential cumulative risk of adverse events of 29% and 46%, respectively.

If this calculation is true, this would encourage the use of aggressive medical therapy for such patients. It is currently impossible, however, to estimate the evolution of risk (especially arrhythmic risk) over time in patients with LVA or LVD.

Study Limitations
Several limitations of the study merit further discussion. First, this study is subject to limitations inherent in retrospective studies. Second, we did not have any information regarding dynamic changes in the ECG, because only one 12-lead ECG tracing was available per patient in the majority of patients. Thus, we cannot report whether these ECG abnormalities worsened over time or whether they might disappear. In the present study, we did not have systematic information on other imaging technologies in the present patients, especially magnetic resonance imaging, which represents an additional limitation. The next step should be a prospective study using a more structured diagnostic work up, also including information from other imaging modalities.

All patients younger than 16 years were excluded from the study, and therefore no comment can be made on young patients with LVA or LVD.

Acknowledgment
None of the authors have any potential conflict of interest to declare.

References