Relevance of Heart Failure in Prevention, Treatment and Prognosis of Ischemic Stroke

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Introduction
According to current estimates, about 1.2 million people in Germany suffer from heart failure (HF). According to data from the German Federal Statistical Office, HF was the second most frequent reason for inpatient treatment in Germany with 432,900 patients treated for HF in 2014 [1]. Chronic HF is also associated with a mortality rate of about 50% within 5 years [2] and is ranked fourth as the cause of death in the German mortality statistics of 2014 [3]. Besides HF with a reduced ejection fraction (HFrEF, ejection fraction < 40%, “systolic” heart failure) and HF with preserved ejection fraction (HFpEF; ejection fraction ≥ 50% “diastolic” heart failure) the current European guidelines introduced the category of heart failure with mid-range ejection fraction (HFmrEF; ejection fraction 40–49%) [4]. HF is found in 13–29% of all patients with acute ischemic stroke and is recognized as the most relevant cardiac cause of ischemic stroke besides atrial fibrillation (AF). This article on the relevance of HF for stroke prevention, acute therapy and prognosis after ischemic stroke is based on a selective literature review and previous publications by the authors [5–7].

Heart Failure as a Risk Factor for Stroke
HF is defined as the inability of the heart to provide the organism with sufficient blood and oxygen to ensure the systemic metabolism at rest and during activity. In addition to impaired left ventricular contractility, HF is associated with a wide range of pathophysiological features including increased platelet activation, reduced fibrinolysis, endothelial dysfunction and increased coagulability, which favor cardiac thrombus formation [5]. Thromboembolic etiology is considered the predominant mechanism of stroke in patients with HF. HF-related hypotension may also contribute to the occurrence of border zone infarctions in the presence of relevant arteriosclerosis. Due to overlapping risk factors of HF and ischemic stroke, however, there are also lacunar strokes or strokes due to large-artery atherosclerosis in HF patients with concomitant atrial fibrillation. This article is based on a selective literature review summarizing the present knowledge as well as current guideline recommendations and provides recommendations for clinical practice.

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ABSTRACT
About 1.2 million people in Germany suffer from heart failure (HF) and HF is present in about 13–29% of all patients with acute ischemic stroke. HF is a risk factor for ischemic stroke and it is accompanied by a comparably high morbidity and mortality after stroke. Only limited data are available regarding the relevance of HF in acute ischemic stroke. The hypothesis has emerged that an acute ischemic stroke may contribute to deterioration and occurrence of heart failure. Stroke prevention by oral anticoagulation is only recommended for HF patients with concomitant atrial fibrillation. This article is based on a selective literature review summarizing the present knowledge as well as current guideline recommendations and provides recommendations for clinical practice.
level also correlated with increased stroke risk in the pooled analysis of the CORONA and GISSI-HF studies [9]. According to a meta-analysis, the risk of recurrent stroke is doubled in stroke patients with pre-existing HF (RR 1.96; 95 % CI: 1.49–2.60) [14]. The underlying, mostly prospective (cohort) studies, however, did not have a uniform definition of HF, reducing the significance of the meta-analysis.

Based on present data, HFrEF has to be considered as independent risk factor for ischemic stroke increasing the risk 2–3-fold. In addition, the risk of recurrent stroke is apparently doubled in (chronic) HF. Comparable data for HfmrEF or HfpEF are not yet available.

**Stroke Prevention in Patients with Heart Failure**

In four randomized trials on stroke prevention in patients with HFrEF (defined as LVEF < 35 %) and maintained sinus rhythm (WARCEF, WATCH, HELAS and WASH), an annual stroke rate of 0.3–1.4 % was found in patients treated with warfarin, acetylsalicylic acid or clopidogrel. However, trial designs were heterogeneous and the HF cohorts were only partially comparable (for overview: 7, 10).

According to a meta-analysis of these four studies, oral anticoagulation with the vitamin-K antagonist (VKA) warfarin reduced the risk of stroke by 41 % (RR 0.59, 95 % CI 0.41–0.85) compared to acetylsalicylic acid. Oral anticoagulation, however, almost doubled the risk of bleeding (RR 2.02, 95 % CI 1.45–2.80) thus canceling the assigned benefit. In addition, there was no difference in mortality, the incidence of myocardial infarction or the rate of hospitalization in this group of patients [15], in which the majority had not suffered from a stroke before enrolment. Further analyses of the WARCEF study showed an increasing risk of (recurrent) stroke in patients with an increasingly reduced LVEF, reaching statistical significance only in patients with LVEF < 15 % [16]. In these patients, there was a trend towards more effective stroke prevention by using acetylsalicylic acid [17]. Due to the low event rates in the WARCEF study, this finding has to be validated in further HF studies.

In four randomized trials on stroke prevention in patients with HFrEF [23]. Relevant data for stroke prevention regarding the use of cardioverter/defibrillators or left ventricular assist devices are not yet available.

Medical primary prevention of stroke in HF patients should be applied according to the individual cardiovascular risk profile. For secondary stroke prevention in HF, acetylsalicylic acid 100 mg once daily should be given in patients with maintained sinus rhythm, while oral anticoagulation is recommended in HF patients with AF.

**Relevance of Heart Failure for Acute Stroke Treatment**

Cohort studies have shown that 13–29 % of all patients with acute stroke have HFrEF and about 9 % of all ischemic strokes are caused by HF [24]. The presence of HF is relevant for cerebral perfusion in the acute phase of stroke since cerebral autoregulation can be impaired and cerebral perfusion is linearly correlated to cardiac output and may be insufficient in the presence of HFrEF. In general, indiscriminate discontinuation of cardiovascular treatment such as antihypertensive drugs or heart rate lowering drugs (in particular β-blockers) should be avoided. Uncontrolled effects such as a sym-
Relevance of Heart Failure for Prognosis after Stroke

Previous cohort studies suggest that stroke patients with pre-existing HF have a two- to three-times higher probability to suffer severe stroke compared to patients without HF [7]. Moreover, in the majority of studies mortality has been observed to be 2–2.5-fold higher in patients with HF compared to patients without HF [5, 31]. Notably, in stroke patients with HF, the risk of dying – which is about 80% over a period of five years – is not further increased in the presence of AF [8, 32]. In turn, the presence of a stroke has relevant implications for the prognosis of HF patients. In patients with HFrEF (in the CORONA study) as well as in patients with HFpEF (in the I-Preserve study) mortality after stroke was significantly higher compared to HF patients without stroke or to patients hospitalized due to worsening of HF [33].

The presence and the characteristics of HF are highly relevant for the prognosis after stroke. Therefore, evaluation of present cardiac function appears to be necessary in patients with acute ischemic stroke. Moreover, attention should be paid to the clinical course of HF. Optimized interdisciplinary care of (stroke) patients with HF is necessary in order to optimize acute therapy and prognosis after stroke.

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Conflict of interests

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