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The role of cardiologists on the stroke unit

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Cardiologists need a better understanding of stroke and of cardiac implications in modern stroke management. Stroke is a leading disease in terms of mortality and disability in our society. Up to half of ischaemic strokes are directly related to cardiac and large artery diseases and cardiovascular risk factors are involved in most other strokes. Moreover, in an acute stroke direct central brain signals and a consecutive autonomic/vegetative imbalance may account for severe and life-threatening cardiovascular complications. The strong cerebro-cardiac link in acute stroke has recently been addressed as the stroke-heart syndrome that requires careful cardiovascular monitoring and immediate therapeutic measures. The regular involvement of cardiologic expertise in daily work on a stroke unit is therefore of high importance and a cornerstone of up-to-date comprehensive stroke care concepts. The main targets of the cardiologists' contribution to acute stroke care can be categorized in three main areas (i) diagnostics workup of stroke aetiology, (ii) treatment and prevention of complications, and (iii) secondary prevention and sub-acute workup of cardiovascular comorbidity. All three aspects are by themselves highly relevant to support optimal acute management and to improve the short-term and long-term outcomes of patients. In this article, an overview is provided on these main targets of cardiologists' contribution to acute stroke management.

Introduction

State-of-the-art stroke care is an interdisciplinary challenge. Stroke is the second leading cause of mortality and the most important cause of disability in adult life.¹ It poses a severe burden on patients, families, and on healthcare systems. With ageing societies and the anticipated further increase of cardiovascular risk factors, a further increase in stroke rates is predictable.

The strong link between multiple cardiovascular pathologies and ischaemic (85% of all strokes) or haemorrhagic (15%) strokes is clearly established. Up to half of the ischaemic strokes are directly related to cardiac and large artery disease and cardiovascular risk factors are involved in most other stroke aetiologies (Figure 1). Virtually any cardiac pathology contributes to increased risk of (cardioembolic) stroke. In fact, a stroke may often be the first clinical event leading to the emergency room (ER) or hospital presentation with a previously undetected cardiac problem as the underlying cause of the acute event. Therefore, it is

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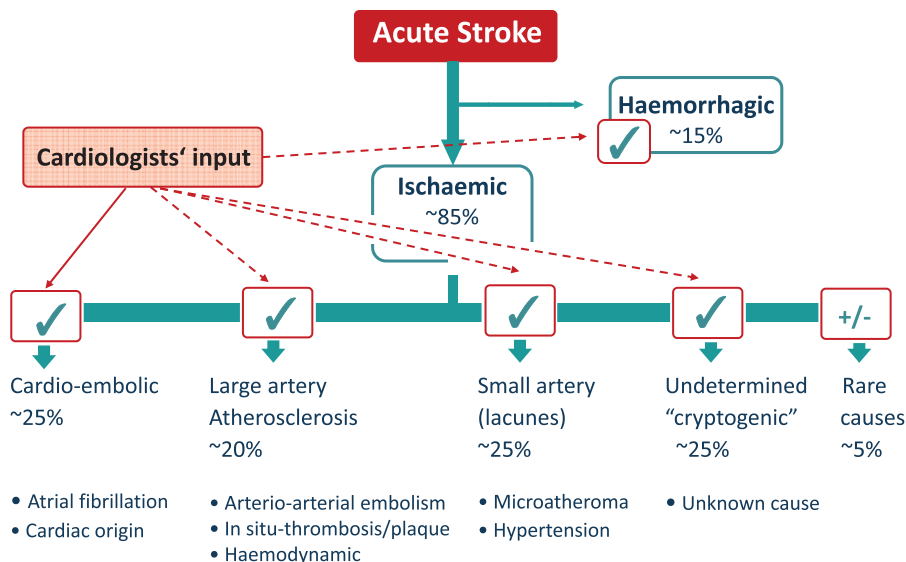


Figure 1: Cardiologists' contribution to stroke care according to stroke aetiology (by Toast classification).

the consensus of the European Society of Cardiology (ESC) cardiovascular round table that cardiologist expertise needs to be integrated on stroke units to address all cardiovascular aspects of acute stroke care² as thorough cardiovascular diagnostic workup is recommended in almost all stroke patients. This may already be started immediately upon medical contact and in ER since the established aetiology of the stroke is vital for further therapy decisions.

Causal therapy

The fast cerebral reperfusion and oxygen supply is the preferred causal therapy in ischaemic stroke as in acute myocardial infarction. Thrombolysis as a well-established therapy and more recently also mechanical endovascular thrombectomy are causal therapies for acute ischaemic stroke. Many efforts have been made in recent years to provide system-wide implementation of these treatment options. Time metrics and advanced patients selection criteria have further improved and resulted in larger proportions of eligible patients and shorter times to treatment. Still, several limiting factors for these therapies remain such as the narrow time windows after symptom onset, multiple contraindications (particularly increased bleeding risks), and limited availability or accessibility (thrombectomy). These therapies are therefore available only for a small proportion of patients (~20-25% of patients are eligible for thrombolysis and ~10-12% of patients for thrombectomy).

Stroke unit care

The major concept—in fact, the backbone of state-of-the-art acute stroke therapy—remains therefore early management on a stroke unit. Stroke unit care is associated with lower rates of disability and reduces mortality after stroke by 24%,³ with a number needed to treat of 20 to improve

functional outcome.⁴ Stroke units are widely available in modern health care systems and all patients admitted to hospital with stroke are eligible for acute treatment on stroke units. While no causal therapy is available in many stroke patients as outlined above, the benefits of specialized stroke units are mainly derived from effective early secondary prevention, from prevention of neurological⁵ and medical⁶ complications in the acute phase of stroke and from early rehabilitation. Cardiologic complications are among the most common complications in acute stroke and require thorough monitoring and sometimes immediate treatment measures. The regular involvement of cardiologic expertise in the standardized stroke care is therefore highly relevant to reduce the risk of complications and to improve the outcomes for patients after stroke.⁷

The cardiologic workup can be categorized according to the clinical question in a systematic concept, as the timing, urgency, and the subsequent clinical decisions may be different depending on these categories.

The main categories of the cardiologic considerations for patients on a stroke unit are (Figure 2):

- 1 diagnostics workup of stroke aetiology,
- 2 treatment and prevention of cardiovascular complications in acute/subacute stroke,
- 3 workup of cardiovascular comorbidity and initiation of secondary prevention.

These categories may well be addressed simultaneously and with the same or overlapping diagnostic methods or monitoring tools. However, this conceptual differentiation is helpful for a systematic framework of cardiovascular involvement in stroke. For instance, an ECG recording may inform about newly detected atrial fibrillation (aetiology of stroke), may further show significant ventricular arrhythmias (complications of acute stroke), and will inform on the choice of secondary prevention (e.g. oral

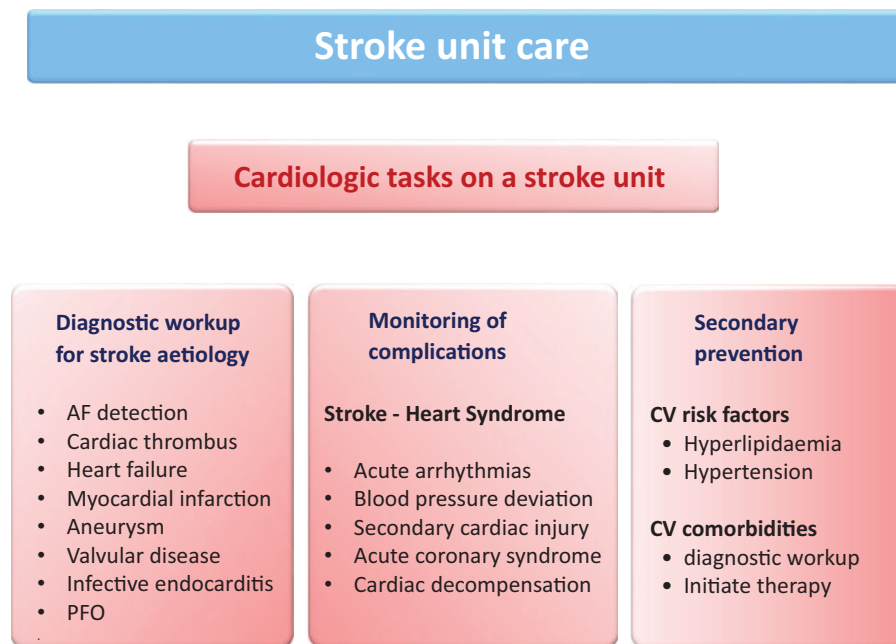


Figure 2: Main categories of cardiologist contribution to comprehensive stroke care on a stroke unit.

anticoagulation). Echocardiography may reveal a thrombus in the left atrium or ventricle (aetiology) and may show a possibly underlying impaired left ventricular function (cardiovascular comorbidity, requiring subsequent cardiac diagnostics and therapy) and may finally result in specific secondary prevention measures [e.g. closure of a persistent foramen ovale (PFO)].

Cardiologists may as well be involved in acute stroke care even before and beside the stroke unit such as in immediate ER therapy, resuscitation, acute thrombectomy intervention, or acute coronary interventions but these aspects are beyond the scope of this paper.

1. Diagnostic workup of stroke aetiology

Identification of the stroke aetiology is of fundamental importance for adequate treatment. While the distinction of ischaemic and haemorrhagic stroke requires cerebral imaging, the further aetiological workup of ischaemic strokes involves a wide range of cardiac and cardiovascular conditions as potential underlying causes of the stroke. Acute and subacute cardiac events may be the underlying cause for a stroke but if this cardiac event occurs oligo- or asymptomatic then the stroke may be recognized as the clinically overt and priority finding. After emergency treatment, the patient is usually transferred to the stroke unit for further therapy with the focus usually on stroke-related symptoms and complications. The adequate diagnosis of co-morbid cardiac events is, however, highly relevant to reduce subsequent complications and to improve functional as well as the prognostic outcomes of the patients. Identification of such constellations requires a sensitivity for cardiovascular sources and mechanisms to complement the neurology-

specific concepts of the stroke unit. Examples for acute cardiac events preceding a stroke are new onset of atrial fibrillation, acute coronary syndrome, acute heart failure, acute dysrhythmia, syncope, and acute valve disorders.

Systematic cardiac evaluation is therefore mandatory in stroke patients. A known **medical history** of cardiovascular disease may inform about increased risk for cardioembolic or vascular events. Risk factors of stroke and coronary artery disease are largely similar, although the relative impact of the individual risk factors may be very different in the coronary and cerebral vascular bed. For instance, the risk due to high cholesterol is less pronounced in stroke than in coronary artery disease and only seen at younger age (40-59 years).⁸ Although an inverse association of cholesterol levels with haemorrhagic stroke has been reported,⁹ cholesterol lowering with statins has become one of the evidence-based treatment in secondary prevention of ischaemic stroke. For assessment of risk factors for secondary prevention, see section "Workup of cardiovascular comorbidity and risk factors for secondary prevention" (below).

Standard cardiac workup for aetiological purpose includes a 12-lead ECG recording, troponin measurement, blood pressure monitoring and continued ECG monitoring on the Stroke Unit for at least 24h, or long-term ECG recording using Holter-ECG, and echocardiography.¹⁰ The workup is based of course on the clinical status, medical history and on stratification of cardiovascular risk factors. An underlying cardiac condition or relevant cardiovascular risk factor may have been undetected so far and becomes only apparent with cardiologic workup of the stroke. This may have immediate implications regarding aetiological determination and subsequent therapy (such as acute newly detected atrial fibrillation, heart failure, myocardial

Table 1: Comparison of transthoracic (TTE) and transoesophageal (TOE) echocardiography for diagnostic workup in patients with stroke. Visual quality: (-) not visible, (+) visibility insufficient, + low, ++ medium, +++ good visibility.

	Transthoracic echo TTE	Transoesophageal echo TOE
Technical characteristics	Longer wave length – Lower visual resolution – Less detail on small structures + Longer range of the image window + Distant parts of the heart	Very short wave length + Very high visual resolution + Assessment of very small structures – Short range of the image window – Probe-near structures only
Procedural characteristics	Non-invasive Simple, fast No strain to the patient Little to no complication	Semi-invasive Requires more time, more personnel Stressful for patient (often sedation required) Potential complications: oesophageal injury, aspiration
Visible cardiac structures/function		
Left atrium (LA)	++	+++
Left atrial appendage (LAA)	–	+++
Atrial septum	++	+++
Atrial-ventricular valves	++	+++
Aortic valve	++	+++
Pulmonary valve	+	+++
Left ventricle (LV)		
LV global dimension	+++	+
LV regional wall structure	+++	+
LV regional contractility	+++	+
LV apex	+++	–
Right ventricle		
RV dimensions	+++	+
RV function	+++	+
Pathologies		
LAA thrombus	(+)	+++
PFO	(+)	+++
ASA	+++	+++
Valvular insufficiency	+++	+++
Valvular stenosis	+++	+++
Valvular structural pathology	++	+++
Infective endocarditis	+	+++
LV dimensions, global function	+++	+
LV regional contractile function	+++	+
LV aneurysma	+++	+
LV thrombus	+++	+
Heart failure (HFrEF and HFpEF)	+++	(+)
Cardiomyopathy	++	(+)
Atrial cardiac tumour	++	+++
Thoracic aorta	+	++
Complex (congenital) defects	++	+++

infarction, infective endocarditis, or PFO). In addition, it may unveil cardiovascular comorbidities that do not necessarily effect acute treatment decisions but may require postponed detailed workup and initiation of adequate cardiovascular treatments (see below).

ECG recording to detect atrial fibrillation (AF) as one of the most common causes of stroke is required with a minimum monitoring period of 24 h. Longer monitoring should, however, be strongly considered in order to identify AF, if no other obvious reason may explain the stroke event. The

ESC guidelines recommend short-term ECG recording followed by continuous ECG monitoring for at least 72 h to screen for AF.¹¹ Detection of AF has significant therapeutic implication, namely the initiation of anticoagulation therapy in order to prevent recurrent strokes. Prolonged ECG monitoring has been shown to result in higher rates of AF detection and anticoagulation initiation.¹² A range of decision algorithms for prolonged rhythm monitoring has been evaluated from repeated Holter monitoring to long-term rhythm monitoring using implanted loop recording devices.

Table 2: Modified Duke Criteria for the diagnostic workup of infective endocarditis [Li *et al.* Ref. 18].

Modified Duke Criteria	
Major criteria	(1) Positive blood cultures ^a 2 or more blood cultures drawn 12 h apart 3 or majority of ≥ 4 separate blood cultures, ≥ 1 hour from first to last (2) Imaging evidence of endocardial involvement Positive echocardiography (TOE) ^b
Minor criteria	(1) Predisposing heart condition/iv drug use (2) Fever, temperature $>38^{\circ}\text{C}$ (3) Vascular phenomena ^c (4) Immunologic phenomena ^d (5) Microbiologic findings ^e
Conclusion on infective endocarditis	
Confirmed infective endocarditis:	2 major criteria 1 major + 3 minor criteria 5 minor criteria
Possible infective endocarditis: ^f	1 major + 1 minor criteria 3 minor criteria
^a Typical microorganisms consistent with IE: HACEK group, <i>Viridans streptococci</i> , <i>Streptococcus bovis</i> , <i>Staphylococcus aureus</i> ; or community-acquired enterococci, or a single positive blood culture for <i>Coxiella burnetii</i> or antiphase I IgG antibody titre 11:800. ^b Oscillating endothelial, valvular vegetation, abscess, pseudoaneurysm, intracardiac fistula, valvular perforation, or aneurysm, new (partial) dehiscence of prosthetic valve. ^c Major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions. ^d Glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor. ^e Positive blood culture but not meeting the major criteria or serologic evidence of active infection with organisms consistent with IE. ^f Requires repeated/extended (novel imaging techniques) diagnostic assessment to confirm or reject IE.	

Given that longer monitoring periods will inevitably result in a higher likelihood of detecting AF, implanted loop recorders may be the ultimate approach to identify patients at risk. There are ongoing debates which patients should receive prolonged ECG recordings and if AF is a foremost marker of atrial cardiomyopathy given the sometimes long time intervals between AF episodes and embolic strokes. Cardioembolic infarct pattern, especially with involvement of more than one vascular territory, older age, elevated cardiac biomarkers such as brain natriuretic peptide (BNP) or troponin, and echocardiographic or ECG risk markers (e.g. large atrial size or high number of supraventricular extra systoles) should prompt prolonged ECG recording.¹³

Cardiac imaging by echocardiography is the pivotal tool to obtain a detailed and current information on the cardiac structural and functional status of the patient. In fact, echocardiography will comprehensively inform all three aspects of cardiac workup (stroke aetiology, acute complications, and cardiovascular comorbidity). Importantly, the two modalities of echocardiography, namely transthoracic echo (TTE) and transoesophageal echo (TOE) provide different insights and address separate questions. Both methods have strengths and weaknesses with regard to the visualized cardiac structures and functions, the procedural effort, invasiveness, strain for the patients, and complication rate. They are not easily interchangeable for the same

information gained and the appropriate method should be selected always based on the specific diagnostic question of the individual case. A summary of the strengths, weaknesses, and of the preferred method respective of the cardiac structure or pathology of interest is shown in *Table 1*.

Other methods of cardiac imaging include cardiac computed tomography (CT) and cardiovascular magnetic resonance imaging (MRI). However, application of these methods in patients with acute stroke is limited to highly specific diagnostics questions as the complexity, patients compliance, and radiation (CT), are relevant limiting factors. Cardiac MRI has been shown to be feasible even in the acute phase after stroke and may allow for myocardial tissue characterization¹⁴ including detection of chronic cardiac ischaemia.

The presence of a persistent foramen ovale (PFO) is a common question in the echocardiographic evaluation of stroke patients when no other cause can be identified (cryptogenic stroke). Strictly, a PFO would only qualify as a permissive factor of a paradoxical embolic event as thrombus formation is required to occur in the venous vascular system. A PFO may be detectable in about 25% of the adult population (up to 30% in younger adults) as a remnant of embryonic circulation rather than a malformation (in contrast to an atrial septal defect). Interventional occlusion of the PFO has been shown to effectively prevent recurrent strokes in a series of recent clinical trials.¹⁵ The evidence

for the efficacy of PFO occlusion is limited to younger patients (60 years or younger). Above this age the likelihood of other mechanisms of stroke (arteriosclerosis, paroxysmal atrial fibrillation) increases, even if undetected in diagnostic workup and hence the procedural risk of the intervention for PFO occlusion may outweigh its benefits in avoiding paradoxical embolism. Also atrial morphology need to be taken into consideration as it has been reported that the presence of an atrial septum aneurysm is a more important predictor of recurrent stroke than shunt size.¹⁶ The treatment decision for PFO occlusion should therefore be made on an individual basis and only after careful diagnostic workup to exclude potential other common aetiologies of ischaemic stroke. A screening for potential causes of embolic formation in the venous circulation should be included (vein thrombosis, lab tests for thrombophilia) but often no underlying mechanism of the thrombus formation may be identifiable.

The suspected presence of acute or subacute infective endocarditis (IE) is a particular challenging clinical constellation. It represents a high risk situation for short-term recurrent strokes and acute cardiac failure and hence for a severe and complicated disease course. Suspicion of infective endocarditis requires meticulous diagnostic workup and early involvement of an endocarditis team.¹⁷ The definite diagnosis is often only available with autoptic findings, the *likelihood* of IE may be evaluated using the modified Duke Criteria.¹⁸ According to these criteria the stroke (vascular embolism) qualifies for merely one (of five) minor criteria (*Table 2*). The diagnosis largely depends on multiple blood culture sampling and echocardiographic evaluation in addition to the clinical findings suspicious of IE. As outlined above, only TOE is sufficiently sensitive to identify or to exclude valvular processes indicative of IE. It is therefore recommended as an emergency diagnostic measure in patients with clinical suspicion of IE. In cases of inconclusive echocardiography, cardiac CT, or ¹⁸G-FDG labelled PET/CT and radiolabelled SPECT/CT have shown to improve the detection of endocardial lesions.¹⁷ These imaging tools may improve the accuracy of the modified Duke criteria.

The diagnosis of a cryptogenic stroke is established when no clear cause of the stroke can be identified. This terminology is, however, controversial as it applies to cases with adequate diagnostic workup as well as to cases with no or insufficient diagnostic workup and even to cases where competing (more than one) causes were identified (e.g. atrial fibrillation and high carotid plaque load). Also, cryptogenic stroke cannot be seen as a regular aetiology of stroke as it merely describes the *absence* of a known aetiology.

There is a clear medical need to address this heterogeneous entity of cryptogenic stroke as it comprises about 25% of patients with ischaemic stroke where a clear treatment decision is precluded by the lack of an identified aetiology. As an attempt to overcome the limitations of the cryptogenic stroke concept, the aetiological category of embolic stroke of unknown aetiology (ESUS) was proposed and a simplified diagnostic algorithm (omitting transoesophageal echocardiography and extensive rhythm monitoring) was suggested to identify such patients.¹⁹ The clinical

Table 3: Cardiac complications during acute stroke

Category	Complication
Arrhythmia	Atrial fibrillation Potential causal role for the stroke Tachycardia or bradycardia Bradycardia (SA block, AV block, bundle block) Supraventricular tachycardia episodes Ventricular arrhythmia
Blood pressure	Hypertensive episodes Hypotension
Myocardial injury	Elevated biomarkers (troponin, natriuretic peptides) Acute coronary syndrome Stress-induced cardiomyopathy
Exacerbation of comorbidities	Acute heart failure decompensation Valvular disease Ischaemic heart disease
Infective endocarditis	Potential causal role for the stroke High risk for recurrent stroke
Prothrombotic complications	Deep vein thrombosis Pulmonary embolism

applicability of the ESUS was tested in two randomized controlled trials (NAVIGATE ESUS and RESPECT ESUS) and in both trials it was observed that the proposed (simplified) diagnostic steps to identify patients with ESUS was not sufficient to support treatment decisions such as anticoagulation.²⁰ A main conclusion from the ESUS clinical trials was that a simplified diagnostic algorithm cannot be recommended. In turn, it shows that a more detailed and individualized diagnostic workup is indispensable for patients with stroke of unclear aetiology. This includes particularly an intensive cardiovascular diagnostic workup such as prolonged rhythm monitoring and sophisticated cardiac and vascular imaging.

2. Cardiac complications in acute stroke

Not only do heart diseases lead to an increased risk of stroke, but in turn the acute stroke may also account for cardiac injury via a range of neurohormonal and vegetative/autonomic signals. This stroke-induced imbalance in vascular and vegetative control accounts for increased electrical and haemodynamic instability and may trigger a range of cardiovascular complications during the acute phase of stroke that require the regular attendance of cardiologists on the stroke unit (*Figure 3*).

Cardiac complications are very common in the acute phase (24-72 h) after stroke, and cardiac monitoring may help to prevent adverse and life-threatening situations. Cardiac causes of death within 3 months after stroke rank second after neurological causes.²¹ It has been

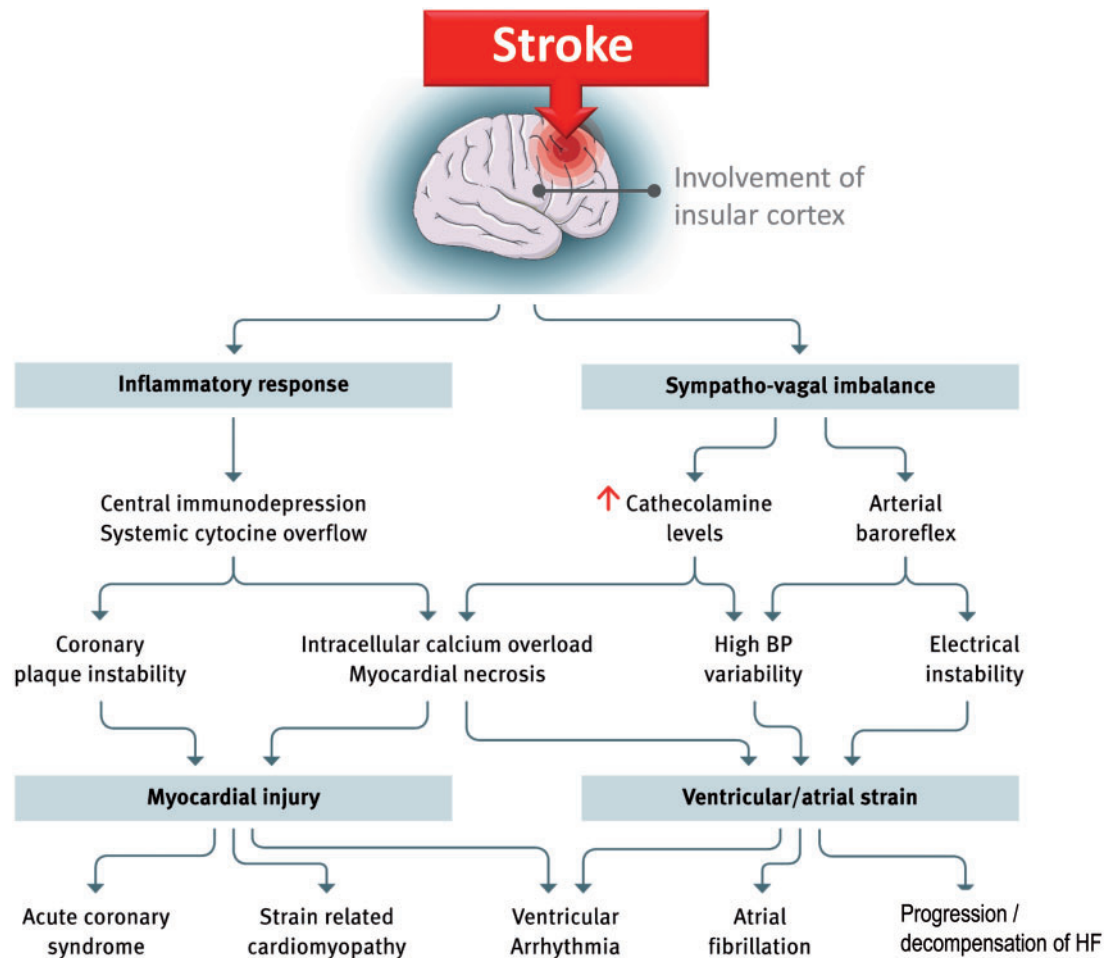


Figure 3: Cerebro-cardiac signalling after stroke, contributing to the Heart Brain Syndrome (modified from reference 24)

demonstrated that mortality after stroke is significantly higher if cardiovascular complications are present.^{22,23} The regular involvement of cardiologists is recommended to address these complications and promote further therapeutic measures if needed. The risk for cardiac complications is even more pronounced in patients with pre-existing cardiac conditions. The neurocardiac signalling as outlined below may account for acute decompensation of a heart disease. Therefore, knowledge of a clinical cardiac history and an up-to-date information on cardiac structures and function from echocardiography assessment are key to be prepared for potential cardiovascular complications or decompensation.

The stroke heart syndrome

There is a broad spectrum of cardiac complications that peak during the first few days after stroke (Table 3). Many patients show asymptomatic or oligosymptomatic ECG alterations or myocardial injury, but some may experience supraventricular and ventricular arrhythmia, critical blood pressure peaks or lows, acute coronary syndrome, or heart failure²⁴ (Figure 3). Older age, higher burden of comorbidities (especially cardiovascular risk factors and chronic kidney disease), and

premorbid cardiac diseases are established risk factors for the occurrence of cardiac complications after stroke. Importantly, there is growing evidence that beside pre-existing cardiac factors and also stroke-related factors have an impact on the occurrence of cardiac complications. Both higher stroke severity and stroke localization involving certain brain areas of central autonomic control (particularly the right insular cortex, but also others) have been strongly linked with stroke-related cardiac complications.²⁵ Given that the spectrum of cardiac alterations show a characteristic pattern in clinical phenotype, risk factors and outcomes, the term 'stroke heart syndrome' has been coined to summarize the characteristic interaction of brain injury and myocardial damage in acute stroke, and to provide a mechanistic framework for clinicians and researchers.²⁶ In brief, the concept of the 'Stroke heart syndrome' considers the acute stroke to exert a 'stress test' to the heart. The 'Stroke heart syndrome' likely originates from stroke-induced disturbance of central autonomic control of the heart with imbalances between the vagal and sympathetic systems.²⁷ In addition, local and systemic inflammatory responses due to the stroke affect the cardiac function. (Figure 3).

Stroke-induced acute myocardial injury

Myocardial injury with elevated cardiac troponin can be observed in up to 50% of patients with acute stroke using high-sensitivity assays.²⁸ These troponin elevations are usually asymptomatic and often reach moderate peak levels when compared with troponin levels observed in acute myocardial infarction. Observational studies suggest that the majority of stroke patients display chronic mild elevation of troponin levels with no substantial rise and/or fall pattern during hospitalization.²⁸ However, neurological deficits and impaired consciousness may mask cardiac symptoms resulting in uncertainty about a potential underlying myocardial injury. Approximately 15-20% of patients with stroke have evidence of acute myocardial injury (including a significant dynamic in troponin levels) that deserves immediate further diagnostic workup. In these cases, type 1 myocardial infarction or type 2 myocardial infarction (e.g. demand ischaemia due to tachyarrhythmia or hypertensive crisis) have to be considered, but also stroke-induced myocardial injury due to a 'Stroke-heart syndrome' should be kept in mind. Acute myocardial injury after stroke may also be due to Takotsubo syndrome. Takotsubo syndrome secondary to stroke occurs especially in elderly women and patients with strokes affecting the insular cortex.²⁹ Of note, there are compelling similarities between the presumed pathophysiology of Takotsubo syndrome and 'Stroke-heart syndrome' with direct catecholamine toxicity and microcirculatory dysfunction.³⁰

The cardiologists role to evaluate clinical presentation, ECG, biomarker dynamics, and cardiac imaging findings is crucial for the interdisciplinary interpretation of elevated cardiac troponin levels. In a small observational study, approximately one quarter of patients with elevated cardiac troponin had evidence of a coronary culprit lesion on coronary angiography, while nearly half of patients had no evidence of coronary artery disease despite elevated troponin.³¹ Patients should be carefully monitored and receive thorough cardiac evaluation to identify co-morbid structural heart diseases, because myocardial injury after stroke is associated with higher short-term and long-term mortality,²⁸ impaired cognitive function,³² and higher risk of future cardiovascular events.³³

Recent insights in troponin dynamics after stroke together with the finding that distinct stroke lesion sites are associated with the extent of acute myocardial injury highlight the notion that direct brain-heart signals contribute to the pathogenesis of acute myocardial injury after stroke. Further studies are needed to determine what proportion of patients with troponin elevation may eventually require further invasive therapeutic measures for acute myocardial injury, and which treatments should be applied in patients with stroke-induced heart injury.

Ventricular arrhythmias

ECG monitoring is not only indicated to identify atrial fibrillation as potential underlying cause for an cardioembolic stroke. In the vulnerable phase after acute stroke electrocardiographic abnormalities (ECG morphology and rhythm abnormalities) occur in up to 90% of the patients.³⁴ Supraventricular and ventricular arrhythmias may occur,

with both tachycardiac and bradycardiac complications which may induce acute haemodynamic instability.⁶ Particularly patients with pre-existing cardiac comorbidities may be susceptible to acute arrhythmias which, in turn, may trigger decompensation of the pre-existing cardiac disease.

Blood pressure

Blood pressure control is challenging in acute stroke care because severe deviation from normal blood pressure control may occur particularly in the first 24-72 h after acute stroke. Critical hypertensive episodes but also haemodynamically relevant hypotension may occur. Such episodes may be difficult to control. Maintaining sufficient cerebral perfusion pressure in the presence of increased intracranial pressure due to cerebral oedema is critical for a good outcome. In patients with *haemorrhagic stroke* careful lowering of blood pressure to <160 mmHg is indicated to reduce haematoma expansion or recurrent bleeding. In turn, in *ischaemic stroke* a U shaped relationship of blood pressure and outcome is reported with lowest mortality related to a medium high blood pressure (150 mmHg) and a higher mortality with both lower and higher blood pressure.³⁵ High blood pressure episodes in ischaemic stroke should be reduced only if blood pressure exceeds 220/120 mmHg in order to maintain blood pressure ≤180/100 mmHg in patients receiving intravenous thrombolysis or in case of acute heart failure. Below these thresholds, high blood pressure is regarded as supportive to maintain cerebral perfusion pressure in the presence of ischaemia-induced cerebral oedema. If, however, thrombolytic treatment for ischaemic stroke is applied, moderate blood pressure lowering may be considered when blood pressure exceeds 185/110 mmHg to prevent haemorrhagic transformation.¹⁰

Heart failure

Heart failure (HF) is a high-risk comorbidity and patients with stroke and with known HF should receive special attention on a stroke unit. Pre-existing HF not only increases the risk of cardioembolic stroke directly (all three factors of the Virchow triad for increased thrombotic activation are activated in HF), HF is often associated with further cardiovascular pathologies (atrial fibrillation, ventricular arrhythmias, valvular diseases, ventricular aneurysm, low cardiac output aggravating sequential carotid stenosis, etc.) which further increase risk for stroke occurrence. Heart failure patients are at higher risk for stroke (stroke prevalence ca 10% in HF populations, stroke incidence two to four times higher compared to non HF patients), HF is also a risk factor for higher mortality of the stroke (two- to four-fold higher), for worse functional outcome of stroke, for a higher risk of recurrent stroke (two-fold higher).²⁴ Interactions between HF and stroke can work in a detrimental way in both directions. The imbalance in neurovegetative control secondary to a stroke may account for acute clinical decompensation of HF via a range of pathways (tachycardia atrial fibrillation, ventricular arrhythmias, blood pressure deviation, or direct myocardial injury, *Figure 3*). Impaired left ventricle systolic function in acute stroke was observed in 24% of stroke patients and 11-18% of

stroke patients were reported with symptomatic HF.²⁴ Treatment of acute decompensation of HF may be more challenging in the subacute phase of stroke as arrhythmias or blood pressure deviations may be more difficult to control in this phase. And in turn, low cardiac output due to decompensating HF will negatively affect the stroke outcome due to reduced cerebral perfusion pressure.

Acute stroke therapy should be pursued irrespective of the HF status but the complication rate may be higher in HF patients compared to non HF. Bleeding risk in rt-PA thrombolysis therapy of stroke was observed almost twice as high in HF patients (OR 1.96, CO 1.3-2.9) compared to non HF patients.³⁶

Currently, there is no sufficient evidence that anticoagulation for stroke prevention is beneficial in patients with HF (and maintained sinus rhythm) is unresolved. After the WARCEF trial showed that anticoagulation with warfarin does not provide a clinical benefit for HF patients,³⁷ the COMMANDER-HF trial also failed to show a convincing benefit of the NOAK rivaroxaban in patients with HF for the composite primary endpoint (death myocardial infarction or stroke; HR 0.91, 95% CI 0.84-1.05).³⁸ Also death from cardiovascular cause or rehospitalization for HF was not improved with the use of NOAK therapy in this trial. The single component of stroke within the primary composite endpoint, however, showed a positive signal for a reduced risk of stroke with the use of rivaroxaban (HR 0.66, 95% CI 0.47-0.95). Further research is needed to clarify if there is a role of anticoagulation for stroke prevention in patients with HF and maintained sinus rhythm.

3. Workup of cardiovascular comorbidity and risk factors for secondary prevention

Pre-existing cardiac conditions are not only a relevant diagnostic finding as underlying cause of the index stroke and as a factor for increased cardiovascular complications in the subacute phase of stroke. Newly detected cardiovascular diseases are also relevant findings as they increase the risk for future acute cardiovascular events including recurrent strokes. Cardiovascular pathologies may be asymptomatic and remain undetected for many years. In fact, the stroke may be the first clinical event to indicate a hitherto undiagnosed or untreated cardiovascular disease.

Therefore, suspected or newly detected cardiovascular diseases need further diagnostic workup and subsequent treatment. Comorbidities such as paroxysmal atrial fibrillation, heart failure, ischaemic heart disease, valvular diseases, arrhythmias, and hypertension may not always receive full diagnostic workup during the stay on a stroke unit and in parallel to acute stroke management. The initial diagnostic steps may therefore require to be followed up after discharge from the stroke unit in subsequent rehabilitation care or in outpatients settings. For this continued diagnostic evaluation the cardiology medicine needs to be accessible, mainly in outpatient settings but for more advanced workup (coronary disease evaluation and intervention, ablation, valve repair, etc) also hospitalized follow-up may be required. It is a common and widely seen observation, however, that the further cardiovascular follow-up

is not pursued to the needed level as stroke patients are often discharged for subsequent treatment to their general practitioner and without further specialized medical attention by cardiology specialists.

Cardiovascular risk factors

A continued monitoring after stroke for cardiovascular risk factors and consequent treatment adjustment over lifetime is recommended to reduce the risk for new cardiovascular events including recurrent stroke. It has been shown that 90% of the population-attributable risk of stroke is accounted for by mere ten key risk factors.³⁹ The most important risk factor for stroke is arterial hypertension, as high blood pressure contributes to both ischaemic and haemorrhagic stroke. Notably, hypertension may be present for years or decades without causing symptoms and therefore the subjective need for diagnostic workup and for adequate treatment may be low on both sides: the patient and the attending physician. Accordingly, the number of patients with undetected hypertension is still very high as is the number of patients with detected but insufficiently treated hypertension.⁴⁰ Further key risk factors are:

- cardiac disease (especially atrial fibrillation)
- diabetes
- smoking
- abdominal obesity
- unhealthy diet
- no regular physical activity
- alcohol consumption
- increased apolipoprotein ApoB/ApoA1 ratio
- psychosocial factors.

Notably, the most important risk factors include high blood pressure, smoking, obesity, physical inactivity, high cholesterol, and diabetes all being modifiable factors that could be targeted in preventive measures. For adequate monitoring and treatment of these cardiovascular risk factors continued specialized medical care including cardiac involvement not only during stroke unit care but on the long-term care of patients after stroke is warranted.

Conclusion

Stroke is a condition requiring interdisciplinary management with the brain-heart axis playing a central role both as causal and complicating factor of stroke. The stroke unit is currently the backbone of state-of-the-art stroke care to prevent acute complications and new vascular events and to improve functional outcome. Treatment and monitoring on a stroke unit are largely driven by the interaction between the brain and the heart as cardiovascular comorbidities and the impaired central control of vegetative/autonomic regulation of the cardiovascular system account for a wide range of acute haemodynamic, electrical, or myocardial complications.

Cardiologist expertise is required in comprehensive treatment concepts for stroke. A more profound understanding among cardiologists and neurologists of the cardiac implication in stroke management will improve integrated stroke care concepts. The supportive cardiology

perspective on stroke patients will support stroke care in several major categories, namely identification of the stroke aetiology, monitoring and prevention of acute and subacute complications, identification of cardiovascular comorbidities and risk factors and establishing long term treatment for secondary prevention. Cardiologists' contribution should be regularly included in the infrastructure of a modern stroke unit.

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