

Cardiovascular care of patients with stroke and high risk of stroke: The need for interdisciplinary action: A consensus report from the European Society of Cardiology Cardiovascular Round Table

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Abstract

Comprehensive stroke care is an interdisciplinary challenge. Close collaboration of cardiologists and stroke physicians is critical to ensure optimum utilisation of short- and long-term care and preventive measures in patients with stroke. Risk factor management is an important strategy that requires cardiologic involvement for primary and secondary stroke prevention. Treatment of stroke generally is led by stroke physicians, yet cardiologists need to be integrated care providers in stroke units to address all cardiovascular aspects of acute stroke care, including arrhythmia management, blood pressure control, elevated levels of cardiac troponins, valvular disease/endocarditis, and the general management of cardiovascular comorbidities. Despite substantial progress in stroke research and clinical care has been achieved, relevant gaps in clinical evidence remain and cause uncertainties in best practice for treatment and prevention of stroke. The Cardiovascular Round Table of the European Society of Cardiology together with the European Society of Cardiology Council on Stroke in cooperation with the European Stroke Organisation and partners from related scientific societies, regulatory authorities and industry conveyed a two-day workshop to discuss current and emerging concepts and apparent gaps in stroke care, including risk factor management, acute diagnostics, treatments and complications, and operational/logistic issues for health care systems and integrated networks. Joint initiatives of cardiologists and stroke physicians are needed in research and clinical care to target unresolved interdisciplinary problems and to promote the best possible outcomes for patients with stroke.

Keywords

Stroke, cardiovascular risk factors, prevention

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Introduction

Stroke is a major burden on patients, caregivers, health-care systems and society. At the beginning of this century, approximately 1.1 million inhabitants of Europe suffered a stroke each year. These numbers are expected to increase by 2025 to 1.5 million owing to the ageing population and persistence of risk factors. Stroke is a major cause of mortality and a leading cause of physical disability, hospitalisation, dementia and depression.¹ Approximately one-third of patients die within a year due to the index stroke, one-third survive with major physical impairment, and one-third have minor impairment but still often face limitations in work and daily life activities. A wide variation of stroke mortality is observed across European countries with a north-south and an east-west gradient ranging from about 300/100,000 inhabitants in eastern European countries to around 60/100,000 in northern and central Europe.² Thus, both the clinical and socioeconomic burden of stroke is high.

Stroke has multiple risk factors, diverse pathophysiology (e.g. ischaemic (approximately 85%), haemorrhagic (approximately 15%)) and various aetiology subtypes (e.g. atherosclerotic, cardioembolic, small vessel disease, rare causes and unknown causes).³ This heterogeneity in risk factors, pathophysiology and aetiology determines the complexity of optimal prevention and treatment strategies, and underscores the challenge of stroke as an acute syndrome.

The brain and the heart are intricately linked in the context of stroke with the heart being both cause and target of stroke pathophysiology and complications. In

state-of-the-art practice, stroke physicians direct the care of patients with acute stroke, with cardiologist expertise being essential for multiple aspects including early causal diagnostic workup, monitoring and management of acute cardiovascular complications. Management of risk factors such as atrial fibrillation (AF), arterial hypertension, valvular and coronary artery disease and long-term secondary prevention all benefit from cardiologist involvement in integrated, interdisciplinary stroke care models.⁴

To promote the interdisciplinary efforts of cardiologists for prevention and clinical treatment of stroke, the European Society of Cardiology (ESC) formed the Council on Stroke. The aim of the council is to improve education, diminish inequalities in clinical standards across Europe, and encourage research. The Cardiovascular Roundtable (CRT), a strategic platform of the ESC to advance health care strategies,⁵ together with the ESC Council on Stroke convened a two-day workshop in March 2018 to identify current and emerging unmet needs and evidence gaps. Renowned experts from multiple specialties involved in stroke care together with European and US-American academic leaders, regulators and experts from industry were invited by the ESC leadership to join the discussion. This paper summarises the targeted priorities and collaborative steps to address the needs of patients at-risk for or already impacted by stroke (Table 1). Comprehensive stroke care and stroke prevention involves multiple other disciplines (e.g. physiotherapy, psychological, nutritional and social care) besides neurologists, neuro-radiologists, cardiologists and vascular surgeons, and for long-term treatment also involves

Table 1. Priorities for cardiovascular research in stroke.**Risk factor management for primary prevention**

- Validate processes to improve implementation of, and adherence to, primary prevention strategies.
- Determine relative importance of risk factors in specific stroke subtypes.
- **Blood pressure:** identify optimal blood pressure targets for prevention of stroke overall, and by stroke subtype and accounting for comorbidities.
- **Cholesterol:** identify target lipid levels relating to stroke subtypes for individualised therapy.
- **AF:** further define and validate the burden of AF (and other atrial arrhythmias)
 - Refine stroke risk.
 - Define needs, timing and specifics of anticoagulation therapy.
 - Define thresholds for the impact of AF burden and how cardiac-implanted electronic devices can help physicians to prevent stroke in at-risk patients.
 - Identify and validate the role of atrial fibrosis and blood stasis in the pathophysiology of AF-related stroke and as potential therapeutic targets.
- Validate wearable technology or mobile health applications for detection of AF and investigate whether arrhythmia detection by these devices leads to a reduction in the risk of stroke.
- Examine the need and added contribution of integrating emerging risk factors in current risk scores.
- Development and validation of bleeding risk scores specifically in AF and in high-risk stroke populations.
- Investigate and validate a precision-medicine approach to antiplatelet therapy in patients with atherosclerotic cardiovascular disease; targeting patients most likely to benefit and least likely to experience harm or non-response.
- Evaluate efficacy and safety of therapeutic alternatives for patients with AF, high ischaemic stroke risk, and contraindications for long-term anticoagulation, e.g. left atrial appendage closure.

Risk factor management for secondary prevention

- Validate a precision-medicine approach to antithrombotic therapy for secondary prevention including dual and combination therapy with NOACs according to individual risk profiles.
- Revision and adjustment to the ESUS concept vs intensified prolonged search for AF.
- Collaborative model of care; dedicated interdisciplinary clinics focused on implementation of secondary prevention strategies.

Acute diagnostics

- Innovations to shorten time between symptom onset and treatment (e.g. combined CT and angiography, mobile stroke unit, angiography only, flat-detector CT).

Acute treatments

- Role of percutaneous thrombectomy in: posterior circulation, basilar artery occlusion; substantial disability (modified Rankin score ≥ 2); large baseline infarcts; NIHSS score ≤ 10 ; longer duration of time since patient last known to be well.
- Evidentiary requirements for new endovascular devices.
- Need for concomitant intravenous thrombolysis and thrombectomy.
- Establishing mechanisms and validate treatment concepts for stroke-induced neurogenic stress cardiomyopathy.

Healthcare systems and integrated networks

- Improving patient access to stroke centres.
- Validate consistent incorporation of cardiology expertise in acute and subacute stroke care.
- Demonstration projects documenting improved patient outcomes, less disability, less socioeconomic burden associated with timely delivery of evidence-based treatments.
- Establishing the benefits of long-term specialised post-stroke care including specialised nurses and cardio-neuro monitoring and risk management.

AF: atrial fibrillation; CT: computed tomography; ESUS: Embolic Stroke of Unknown Source; NIHSS: National Institutes of Health Stroke Scale; NOAC: novel anticoagulation.

general practitioners and geriatricians, but these topics are outside the scope of this article and not discussed herein.

Causality, prevention, and risk factor management

Risk factor management for primary prevention

Primary prevention of stroke involves both screening for and treatment of major risk factors including hypertension, AF, arteriosclerotic artery disease, elevated

blood cholesterol levels as well as lifestyle factors such as smoking, alcohol, physical inactivity or obesity; and other risk factors such as diabetes mellitus, health related quality of life, or a family history of stroke or AF.⁶ Poor control of these risk factors has been reported in general populations,⁷ as well as in patients with ischaemic stroke. Gender differences in stroke are incompletely understood, low testosterone levels have been observed with increased risk of AF and hence ischaemic stroke in men but not in women.⁸ It is acknowledged that implementation of primary

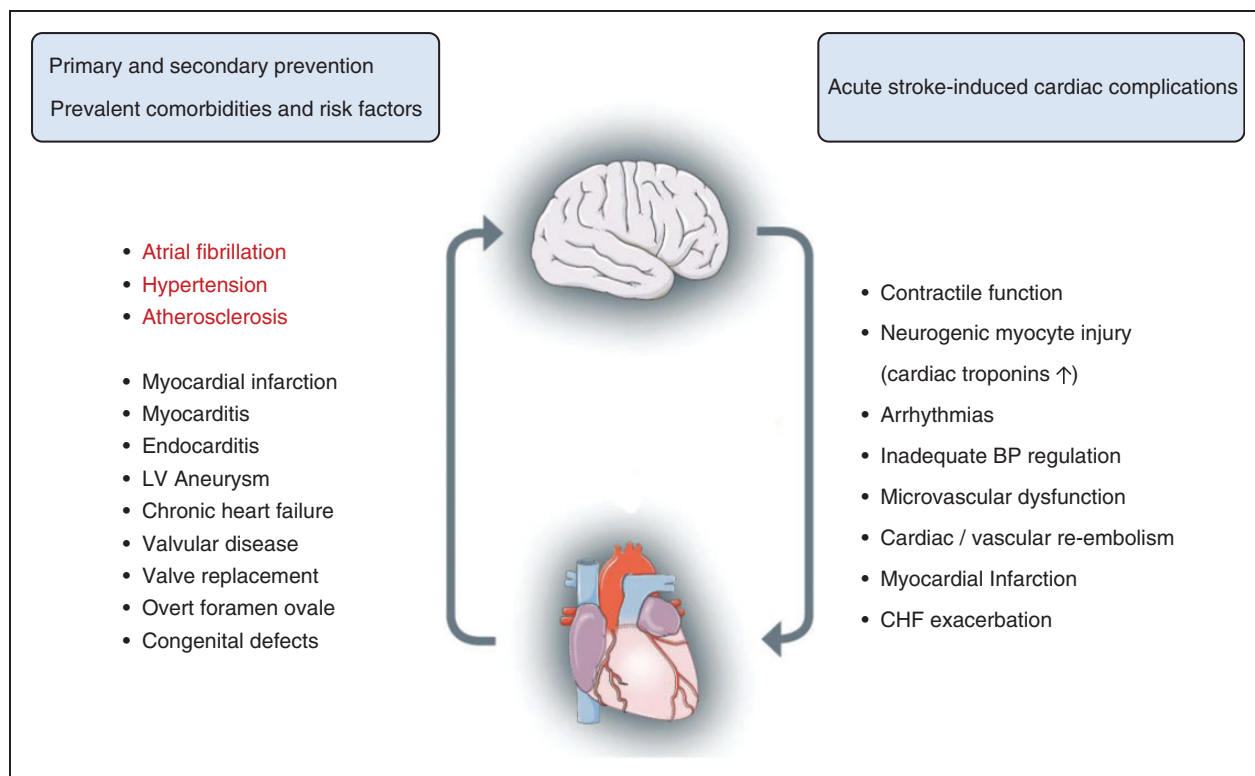


Figure 1. The cardio-stroke interaction for prevention and treatment of stroke and related complications.

Cardiac diseases and injuries can be both cause and consequence of stroke. Cardiac pathologies may often remain undetected with the stroke being the first clinical incident. Cardiovascular diagnostic work-up and monitoring of cardiovascular complications in acute and subacute stroke require involvement of cardiologic expertise in the interdisciplinary team for state of the art stroke care. LV: left ventricle; BP: blood pressure.

prevention strategies may be more difficult than initiatives for secondary prevention, owing to a broader target population and less well-defined patient groups. Almost any cardiac pathology may account for an increase in the risk of stroke, yet stroke may often be the first clinical event of a previously undetected cardiac disease that requires further diagnostic and treatment measures (Figure 1).

Blood pressure. Arterial blood pressure is the most important risk factor for both ischaemic and haemorrhagic stroke, and lowering blood pressure reduces the risk of stroke, irrespective of the pre-treatment blood pressure level.^{9,10} Targets for blood pressure levels as recommended by the guidelines of the European Society of Cardiology/European Society of Hypertension are 120–129 mm Hg in most patients <65 years of age and 130–139 mm Hg for patients ≥65 years of age.¹¹ Recent evidence, however, may challenge such global blood pressure targets as the risk associated with hypertension may depend on a wider range of interrelated factors including not only age but also type of stroke, comorbidities and cardiovascular risk profile.¹² Further uncertainty exists on the

blood pressure variables that need most attention, i.e. absolute blood pressure, pulse pressure, as well as isolated systolic or diastolic blood pressure elevations or diurnal trends.¹³ Owing to the log-linear relationship between blood pressure and stroke incidence, the choice of a specific blood pressure target to prevent a stroke is not supported by strong evidence.

Despite the clear understanding that uncontrolled hypertension is a strong risk factor for stroke, there is still an unacceptably high prevalence of undetected hypertension as well as of detected but not treated or not effectively treated hypertension. Further research and educational work is clearly needed to target this modifiable risk factor.

Cholesterol. Cholesterol is a strong risk factor for ischaemic heart disease and myocardial infarction (MI). In ischaemic stroke, however, the impact of cholesterol is less clear as the association of high cholesterol and mortality risk is much weaker and only seen at younger ages (40–59 years). Lowering total cholesterol is associated with a lower risk of ischaemic stroke but relates to a marginally greater risk of haemorrhagic stroke in some series.¹⁴ Again, this observation also varies by

age. These findings are consistent with the effects of statin and proprotein convertase subtilisin kexin 9 (PCSK9) inhibitor therapy on lowering the risk of ischaemic, but not haemorrhagic stroke. Genome-associated studies further suggest specific patterns in risk factors and pathophysiology depending on the subtype of stroke. Accordingly, a weak association between low-density lipoprotein cholesterol (LDL-C) and ischaemic stroke has been observed for large artery atherosclerosis strokes, but not for small artery occlusion or cardioembolic stroke subtypes.¹⁵ Knowledge of the primary pathophysiology of plaque load in an individual patient may enable more precise targeting of individual risk factors and prevention strategies.¹⁶ The optimum treatment regimen balancing efficacy on stroke aetiology and accounting for patient specific susceptibility has yet to be determined.

Atherosclerotic cardiovascular disease. Patients with symptomatic atherosclerosis, for example those with carotid artery disease or a prior MI, are also at increased risk for atherothrombotic stroke. This underscores that pathophysiology and risk factors for atherosclerosis in the coronary and cerebral vasculature are similar (e.g. elevated cholesterol, smoking, lifestyle factors) albeit substantial differences as to the strength of impact may exist.¹⁷ Whilst intervention for symptomatic and asymptomatic¹⁸ carotid stenosis is beneficial for long-term stroke prevention, medical treatments, including antiplatelet therapy in patients with atherosclerotic cardiovascular disease, reduce the risk of stroke. In fact, substantial evidence has been accumulated on the efficacy of antiplatelet therapy to prevent repeated ischaemic events (see also below for secondary prevention). Interventional concepts for carotid vascular disease (i.e. endarterectomy vs carotid stenting) depend on meticulous measures of quality control, high volume centres and adequate patient selection, and are a matter of ongoing studies.

Some evidence suggests that more intense therapy (such as aspirin in combination with ticagrelor) is more effective to reduce the risk of stroke than low dose treatment with aspirin alone.¹⁹ More robust evidence, however, on optimum dosing, intensity and duration of antiplatelet therapy in patients with atherosclerotic disease is warranted from ongoing trials (ANDAMAN (ClinicalTrials.gov identifier: NCT0252092), ADAPTABLE (ClinicalTrials.gov identifier: NCT02697916)). Uncertainty exists particularly in patients with low cardiovascular risk profile as the potential benefit of antiplatelet therapy is less pronounced and may be increasingly outweighed by the risks of bleeding. Accordingly, recent trials have further challenged the net benefit of aspirin in primary prevention (ASPREE (ClinicalTrials.gov identifier:

NCT01038583), ASCEND (ClinicalTrials.gov identifier: NCT00135226)). Notable, discrepant guideline recommendations on the use of antiplatelet therapy in patients with low cardiovascular risk are given in Europe and the USA which underscore the need for further evidence.

Atrial Fibrillation (AF). AF is associated with an increased risk for cardioembolic stroke, but the debate is ongoing as to whether this is a causal factor or simply a risk marker of more complex atrial cardiomyopathy. Despite the wealth of data and mechanistic models, the patterns and burden of AF that increase the risk of cardioembolic stroke are not well understood.

The risk of stroke appears to be higher in permanent or persistent AF than in paroxysmal AF.²⁰ However, in paroxysmal AF clinicians still lack an evidence-based threshold for defining the absolute time burden of AF where stroke risk is increased. Currently thresholds from 30 s to 6 min, 5.5 h and up to 24 h and longer are discussed in this context. The often substantial dissociation of recorded AF episodes and embolic events further challenge the hitherto understanding of stunned atrium to mechanistically explain thrombus formation. In addition to AF, other atrial arrhythmias, including frequent supraventricular ectopic activity or subclinical atrial tachycardia, are associated with an increased risk of ischaemic stroke. Methods and length of heart rhythm monitoring have been investigated intensely. Prolonged electrocardiographic monitoring in patients who had a stroke increases the detection rate of AF;²¹ however, whether this translates into a reduction in the future risk of stroke is not known. Implantable cardiac monitor devices seem to provide the ultimate option for continued monitoring for AF burden but efficacy and practicability needs to be evaluated in combination with shorter and less invasive monitoring strategies. Emerging wearable consumer devices such as the smart watch and many others yield great potential in the context of rhythm monitoring. Further studies will show if such devices may be applicable for clinical use for AF detection.

The concept of atrial myopathy is increasingly discussed as a pathophysiological concept of thrombus formation resulting from complex atrial injury, wall stress, local inflammation and fibrosis which leads to atrial structural remodelling and increased thrombogenic potential. While atrial fibrosis has been addressed as a major factor in this process, underlying mechanisms, clinical application and adequate measurement tools or biomarker assessments are currently unclear.²² More work is needed to further characterise whether AF or the underlying atrial cardiomyopathy is the greatest contributor to stroke risk.

The CHA₂DS₂-VASc risk score is widely used and guidelines are recommended for stroke risk prediction

in patients with AF taking into account individual patient characteristic comorbidities. While the cumulative impact of confounding factors is well reflected in the score, uncertainty exists as to the borderline risk constellation of CHA₂DS₂-VASc score of one.²³ Incomplete data exist and need further validation as to whether, and which, anticoagulation strategy can be recommended at this low risk level.

Risk factor management in secondary prevention

Management of risk factors. As a general approach, after the acute event of stroke, stroke patients should be recognised as chronic patients, requiring chronic management of stroke sequelae, risk factors and comorbidities to improve the long-term outcome, to prevent recurrent stroke events as well as cardiovascular events. Cardiovascular events are common after stroke and are the leading cause of death one year after an index stroke.²⁴

The implementation of, and adherence to, risk factor management after stroke is suboptimal with substantial inequalities between countries in Europe. While structured and individualised rehabilitation concepts are implemented in continued healthcare structures in some countries, no such structured rehabilitation is available in others. Stroke patients are often discharged to primary care physicians without structured follow-up of their cardiovascular condition. By contrast, a systematic, interdisciplinary approach would be needed combining the expertise of cardiologists, stroke physicians and other specialties for rehabilitation and management of risk factors, cardiovascular complications and comorbidities with continued monitoring and therapy of patients after stroke (Figure 2). Ideally, cardiovascular diagnostic work-up led by cardiologists should be started immediately at the index event hospitalisation and should continue if needed after discharge to assess the risk profiles and create a treatment plan that targets prevention of both recurrent stroke and cardiovascular events. Secondary prevention clinics staffed by specialty trained nurses and, potentially, other health allied professionals may be a tool to achieve better implementation of and adherence to secondary prevention strategies (e.g. blood pressure and cholesterol reduction, smoking cessation, anticoagulation in AF). Such collaboration between cardiologists, specialty nurses and stroke physicians may be a key to achieving the European Stroke Organisation's (ESO) Action Plan for Stroke, which specifically emphasises the importance of secondary prevention and organised follow-up.²⁵

Antiplatelet therapy. Antiplatelet therapy improves outcome in patients with acute ischaemic stroke and transient ischemic attack (TIA), primarily by preventing early recurrence of stroke.²⁶ However, a risk of

secondary bleeding into infarcted tissues is greater for larger infarcts and with early administration of antiplatelet therapy. Combinations of dual antiplatelet therapy or antiplatelet therapy with novel anticoagulation (NOAC) therapy are subject to recent and ongoing investigations.²⁷ Different treatment regimens in patient cohorts with overlapping risk profiles yield beneficial results such as dual anti platelet therapy in patients with cerebrovascular ischaemic event (POINT (ClinicalTrials.gov identifier: NCT0099102))²⁸ or antiplatelet plus NOAC therapy in patients with cardiovascular ischaemic disease (COMPASS (ClinicalTrials.gov identifier: NCT01776424)).²⁹ Further work is needed to clarify the optimum treatment strategies in individual risk- and comorbidity settings for easy clinical use.

Emerging data suggest different stroke subtypes may respond differentially to antiplatelet agents, with atherosclerotic stroke particularly benefitting from more intensive antiplatelet therapy in the first few weeks after the event,³⁰ while small artery stroke had a worse outcome with aspirin and clopidogrel than aspirin alone, showing no reduction of ischaemic stroke and an increased bleeding risk.³¹ Future trials are warranted to focus on a precision medicine approach to identify patients who have the greatest likelihood of benefit and least likelihood of harm.

The Embolic Stroke of Unknown Source (ESUS) concept. In contrast to extended monitoring for AF in patients with cryptogenic stroke, the ESUS concept was recently tested as an approach of minimal diagnostic workup followed by rapid implementation of anticoagulation therapy. Two major clinical trials (NAVIGATE-ESUS (ClinicalTrials.gov identifier: NCT02313909),³² RESPECT-ESUS (ClinicalTrials.gov identifier: NCT02239120))³³ could, however, not show superiority of this simplified diagnostic workup. This challenges the underlying hypothesis that the majority of occurrences of ESUS would be caused by cardioembolic events, and that limited diagnostic workup may be sufficient for a one-size-fits-all-type of anticoagulation therapy. Clearly, more thorough and individualised cardiac diagnostic workup is needed to identify underlying pathology and appropriate therapy for those patients. These results require further evaluation and interpretation in the context of somehow contrasting findings in the COMPASS trial (beneficial effect of NOAC therapy in patients with ischaemic heart disease) but similar findings in the COMMANDER HF trial (no benefit of NOAC in Heart failure patients).³⁴ More evidence from ongoing trials (ATTICUS (ClinicalTrials.gov identifier: NCT02427126), ARCADIA (ClinicalTrials.gov identifier: NCT03192215)) is awaited to inform the ongoing discussion on the applicability of the ESUS concept.

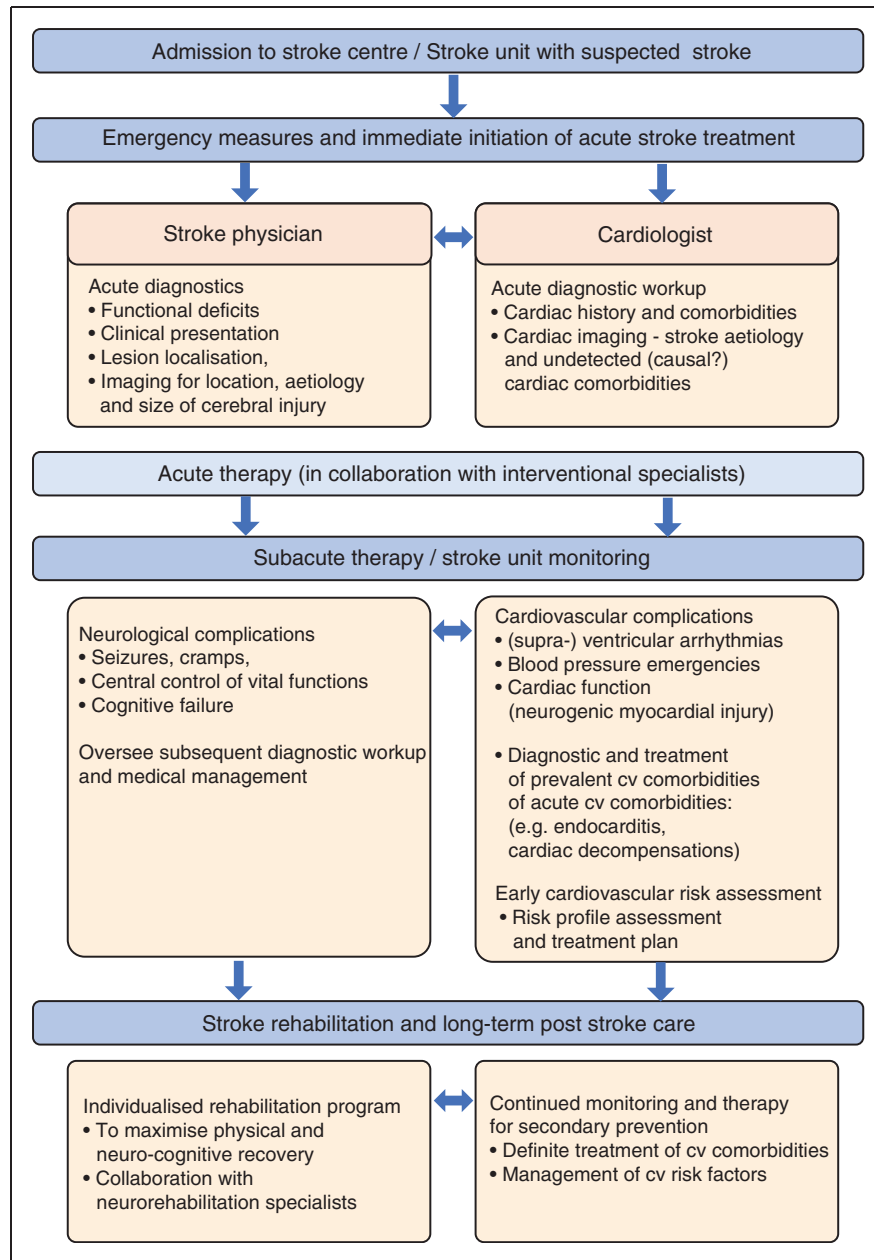


Figure 2. Interdisciplinary delivery of stroke care. While inpatient management is overseen by stroke physicians, early and continued support should be provided by cardiology consultation as a consistent component of an integrated care model through all phases of stroke care for acute and subacute therapies, diagnostic workup, handling of cardiovascular complications of stroke and secondary prevention. Follow-up after discharge by both specialties is recommended, with support from a cv secondary prevention clinic to ensure implementation of and adherence to secondary prevention strategies. Secondary prevention can be provided by primary care, if available, or a specialty nurse-directed clinica for risk factor management can be envisioned for this purpose. cv: cardiovascular.

Occlusion therapies for persistent foramen ovale and left atrial appendage

For patients with AF and a high risk of ischaemic stroke who have contraindications for long-term anticoagulation, other approaches for stroke prevention need to be explored. Occlusion of a patent foramen

ovale has been shown in recent trials to yield beneficial results in patients with cryptogenic stroke yet optimum patient selection for this novel invasive therapy and timing is still a matter of ongoing debate. Left atrial appendage closure has been suggested as a potential therapeutic option. However, more data are needed to establish the clinical efficacy and safety of this approach

(current ESC guideline class of recommendation IIb, level of evidence B).³⁵ Two larger trials of left atrial appendage closure in patients with high ischaemic and very high bleeding risk are currently ongoing (CLOSURE-AF (ClinicalTrials.gov identifier: NCT03463317), STROKECLOSE (ClinicalTrials.gov identifier: NCT02830152)).

Acute stroke

Percutaneous thrombectomy

Percutaneous thrombectomy is a relatively new treatment for acute stroke. Data from five trials of second-generation neurothrombectomy devices in 1287 patients with stroke due to large vessel occlusions showed that this therapy significantly reduced disability at 90 days.³⁶ Not addressed in these trials were patients with posterior circulation occlusion, substantial disability (modified Rankin score ≥ 2), and large baseline infarcts. Uncertainty remains about a number of specific aspects of this novel therapy such as the adequate and maximum time windows, optimum combination with thrombolytic therapy, and accessible vascular territories.

Mechanical thrombectomy therapy is in a very early stage of clinical implementation, and further studies and clinical experience are warranted to explore the full potential of catheter intervention for brain ischaemia. The advances with mechanical thrombectomy may resemble the evolution in percutaneous coronary intervention, from balloon angioplasty in the 1980s to bare metal stents in the 1990s and drug-eluting stents in the 2000s.

Treatment of stroke-induced cardiovascular complications

Cardiovascular complications are common in the early post-stroke period and are a major reason to explain the benefit of stroke unit care in the subacute phase after stroke. These events may represent a stroke-specific pattern of a neurogenic heart syndrome where severe imbalances in sympathetic and parasympathetic activity and peripheral reflex circuits lead to cardiovascular dysregulation such as hypertensive crises, coronary vasospasm, supraventricular or ventricular arrhythmias, contraction band necrosis or takotsubo-like cardiomyopathy (Figure 1).³⁷ Cardiologist expertise should be present in stroke unit settings as a consistent component of an integrated care model to address the multiple cardiovascular aspects of post-stroke care. These may include arrhythmia management, blood pressure control (both hypertensive crisis and hypotension), elevated cardiac troponin (which are often not due to culprit coronary lesions), endocarditis

and general management of cardiovascular comorbidities (heart failure,³⁸ valvular disease, chronic ischaemic coronary artery disease).⁴ The management of these cardiovascular conditions often extends beyond the acute phase and should be continued in chronic care settings (see also next chapter). Collaboration of medical societies across clinical specialties is needed to create consistent guidelines for the management of cardiovascular conditions in the setting of acute stroke.

Integrated healthcare systems and networks

In ischaemic stroke, time dependency of treatment initiation is a crucial factor to determine treatment efficacy and outcome. Systems of care must be designed to minimise delays in assessment and initiation of treatment. New imaging modalities may be one method that can promote efficiencies in the system and reduce treatment delays.³⁹

Patient access to stroke care varies widely among countries in the European Union (EU), and even within regions of a single country, hence major inequalities exist in availabilities of stroke unit care, intravenous thrombolysis and endovascular therapy. Stroke unit numbers range from 1.5–5.8 stroke units per 1000 annual incidents, estimates of mean annual numbers for intravenous thrombolysis ranged from 72–205 per 1000 annual incidents and for endovascular treatments ranged from 19–56 per 1000 annual incidents.⁴⁰ Interdisciplinary consensus guidelines are warranted to recommend a minimum standard of care that should be provided to all patients, regardless of country. Such recommendations may help minimise the disparities in stroke care that currently exist in the EU, and they would be a helpful resource for professional organizations who are working with health authorities to improve timely patient access to stroke centres. The European Society of Cardiology is committed to partnering with the ESO, European Society of Minimal Invasive Therapy (ESMINT), European Society of Vascular Surgery (ESVS) as well as with national societies, and local health authorities to develop these minimum standards and ensure their effective implementation across the EU.

Conclusion

Many advances in stroke care have been achieved, resulting in better patient outcomes and decreased mortality. Interdisciplinary concepts of modern stroke care call for consistent and structured involvement of cardiovascular expertise in diagnostics, acute and subacute therapy, primary and secondary prevention and follow-up measures in stroke. Many gaps in evidence remain and have been identified as targets for further initiatives.

These gaps present challenges as well as opportunities to clinicians, researchers, industry, and professional organizations to improve stroke care and reduce its associated burden. Cardiologists and stroke physicians should communicate closely and in collaboration with industry to further develop the tools, resources and treatments that would be useful for improving efficiency and reducing the time to treatment. Such communication will help to drive innovations in the identified areas of greatest need. The ESC is determined to promote interdisciplinary collaboration and to pursue integrated care strategies by driving activities of clinical education and scientific exchange, encouraging research, and fostering guideline development towards comprehensive concepts of stroke prevention and treatment.

Author contribution

WD, MM, BH and DL contributed to conception and writing of the paper, GH, EAB, RAB, AJC, BC, VC, CC, HCD, ME, PG, AH, JCH, DRJ, AK, MK, AK, UL, HSM, GN, FRP, MR, GMCR, MR, MS, RMT and PW contributed to writing and critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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