"Novel Clinical Concepts in Thrombosis": Integrated Care for Stroke Management—Easy as ABC

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Introduction

Stroke care often involves a multidisciplinary effort, including the stroke physician, internist, neurologist, interventionist, cardiologist, radiologist, vascular surgeon, neurosurgeon, emergency room physician, primary care physician, general practitioner, and rehabilitation team (including physiatrist and therapists), as well as nurses, patient carers, and next of kin (►**Fig. 1**). Ultimately, the patient is central to all this, receiving information from different health care professionals. The patient "journey" requires a simple and uniform approach to the priorities of poststroke management, which can be uniformly and consistently described by different health care professionals, allowing patient (and carer) engagement and empowerment with regards to their care.

Such an "integrated care" approach has been applied in other chronic conditions. For example, the ABC (Atrial fibrillation Better Care) pathway has been proposed as an integrated approach to improve the management of patients with atrial fibrillation (AF). This has three central pillars: "A"—avoid stroke (with anticoagulants); "B"—better symptom management, with patient-centered decisions on rate or rhythm control; "C"—cardiovascular and comorbidity risk optimization.[1] This concept was first proposed to promote a streamlined approach to management that can be applicable to whether the AF patient is managed by any health care professional, the general practitioner, or the hospital-based specialist (whether cardiologist or noncardiologist).

This integrated care approach to AF management is promoted in patient pathways to improve diagnosis and management of AF patients, and would facilitate discussion and patient engagement on the principles of AF care ("easy as ABC…") and importantly, minimizes the possibility of conflicting information from health care professionals. Such conflicting information when dealing with patients has been associated with poorer patient adherence with their management plan.[2]

The ABC pathway has been well validated in posthoc analyses of clinical trials, prospective cohort studies, and a prospective randomized trial. In a recent systematic review, AF patients treated according to the ABC pathway showed a lower risk of all-cause death (odds ratio [OR]: 0.42, 95% confidence interval [CI]: 0.31–0.56), cardiovascular death (OR: 0.37, 95% CI: 0.23–0.58), stroke (OR: 0.55, 95% CI: 0.37–0.82), and major bleeding (OR: 0.69, 95% CI: 0.51–0.94).[3] Improved clinical outcomes with ABC pathway compliance are evident, even in clinically complex patients such as those with multimorbidity, polypharmacy, and hospitalizations.[4]

The mAFA-II trial was a prospective cluster-randomized trial of patients randomized to receive usual care, or integrated care based on the ABC pathway.[5] Rates of the composite outcome of "ischemic stroke/systemic thromboembolism, death, and rehospitalization" were lower with the mAFA intervention compared with usual care (1.9 vs. 6.0%; hazard ratio [HR]: 0.39; 95% CI: 0.22–0.67; $p < 0.001$). Rates of rehospitalization were also lower with the mAFA intervention. In the mAFA-II trial long-term extension cohort, these beneficial effects were maintained, and there was a high adherence (>70%) and persistence (>90%) with the mAFA app-based intervention based on the ABC pathway.[6] The mAFA-II trial also reported that this holistic app-based management with dynamic risk monitoring and reassessment of the bleeding risks (using HAS-BLED score) reduced the risks of major bleeding (mAFA vs. usual care, 2.1 vs. 4.3% at 1 year) and increased total oral anticoagulation (OAC) usage from 63 to 70%.[7]

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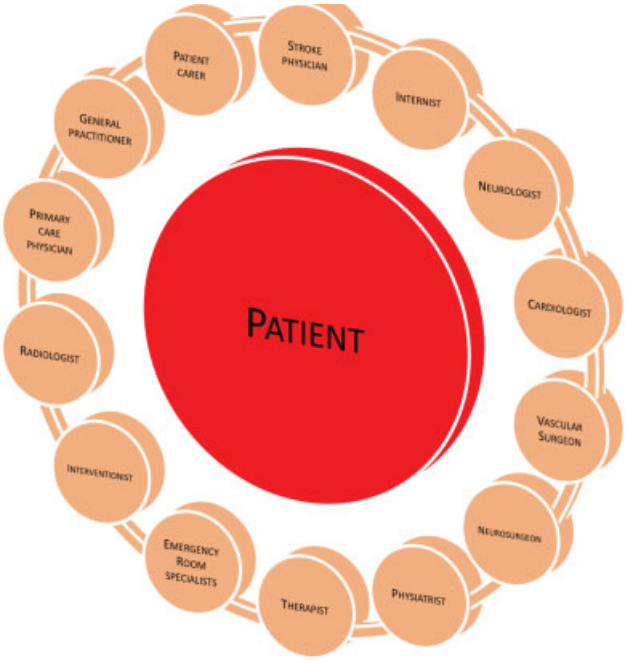

Fig. 1 Stroke: multidisciplinary approach and integrated care for a syndrome with complex etiology, diagnostics, intervention, rehabilitation and prevention.

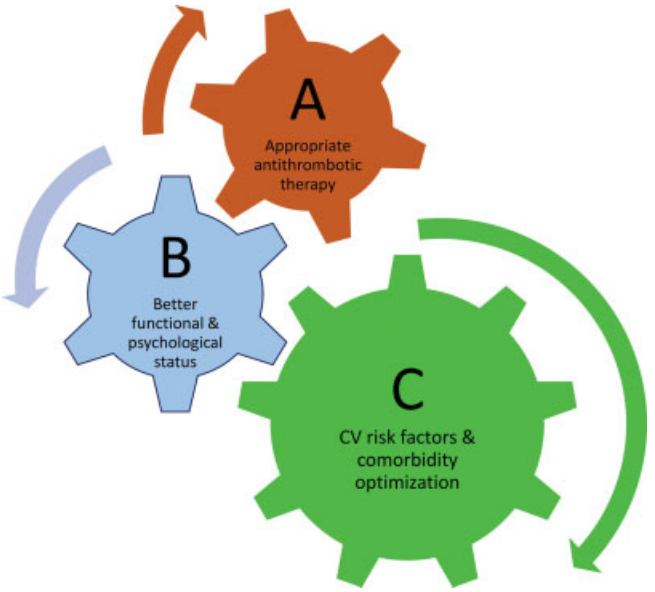

Fig. 2 The post-stroke ABC pathway: a holistic approach to integrated stroke care with three key objectives.

An ABC Pathway for Poststroke Care

Both AF and stroke share common cardiovascular risk factors, including advancing age, male sex, hypertension, diabetes mellitus, valvular heart disease, heart failure, coronary heart disease, chronic kidney disease, inflammatory disorders, sleep apnea, and tobacco use.[8] Therefore, a more integrated or holistic management pathway is also needed for patients following a stroke, that not only targets the prevention of recurrent stroke, but also improves patient functional status and symptoms, and manages cardiovascular comorbidity risk. Some preliminary data suggest improvements in functional status with a multidisciplinary approach to care after stroke.[9]

The aim of this "novel clinical concept" article is to propose a poststroke ABC pathway as a more holistic approach to integrated stroke care, which includes three key objectives (►**Fig. 2**):

- A: Appropriate Antithrombotic therapy.
- B: Better functional and psychological status.
- C: Cardiovascular risk factors and Comorbidity optimization (including lifestyle changes).

Appropriate Antithrombotic Therapy

In the poststroke patient, the "A" step refers to the use of anticoagulants when AF or a mechanical heart valve is present, or antiplatelets when there is associated atherosclerotic vascular disease and no AF or mechanical valve. Even then, a balance is needed between preventing recurrent ischemic events and major bleeding.[10,11]

The challenge in the stroke patient is what to do if there is both AF and vascular disease, whether coronary, carotid, or peripheral artery disease. Data from the randomized trials in patients with AF suggest that anticoagulation alone would suffice in stable vascular disease—OAC, either as a non-vitamin K antagonist OAC (NOAC; also called a direct OAC or DOAC) or well-managed vitamin K antagonist (e.g., warfarin) with a time in therapeutic range $\geq$70%.[12]

However, many physicians would still prescribe combination therapy, despite the paucity of evidence from large randomized trials. In a systematic review and meta-analysis, the pooled prevalence of carotid stenosis in AF patients was 12.4% (95% CI: 8.7–16.0), ranging from 4.4 to 24.3%.[13] Also, nonstenotic carotid disease may be present in about half of AF patients. In such AF patients there is a balance between preventing stroke due to AF, which requires OAC, and preventing stroke due to vascular disease, which in the non-AF setting usually requires antiplatelet therapy.

In AF patients with coronary artery disease, appropriate antithrombotic therapy management varies according the clinical scenario.[14] In the AF patients presenting with an acute coronary syndrome (ACS), there needs to be a balance between AF-related stroke prevention which requires OAC, reducing cardiac ischemia in an ACS presentation which requires antiplatelet therapy, minimizing the risk of stent thrombosis after a percutaneous coronary intervention, and the risk of bleeding by the combination of OAC with antiplatelet therapy.[15] When the AF patient has "stable vascular disease" (arbitrarily defined as >12 months without acute issues), the patient should be managed with OAC monotherapy, as evident from a systematic review and meta-analysis of observational data,[16] and the AFIRE trial, where combination therapy with OAC plus antiplatelets was associated with worse thromboembolic and bleeding outcomes in AF patients with stable vascular disease.[17]

In high-risk stable atherosclerotic vascular disease patients *without AF*, the COMPASS trial[18] showed that the

primary outcome (composite of cardiovascular death, stroke, or myocardial infarction) was lower in the low-dose rivaroxaban-plus-aspirin group compared with the aspirin-alone group (HR: 0.76; 95% CI: 0.66–0.86), at the risk of more major bleeding events (HR: 1.70; 95% CI: 1.40–2.05). Mortality was also lower in the rivaroxaban-plus-aspirin group compared with the aspirin-alone group (HR: 0.82; 95% CI: 0.71–0.96). Of the secondary outcomes, ischemic stroke was significantly lower with combination therapy (HR: 0.51; 95% CI: 0.38–0.68) compared with aspirin, and with rivaroxaban alone versus aspirin (HR: 0.69; 95% CI: 0.53–0.90).[18] Hence, in high-risk vascular disease patients, combination therapy with rivaroxaban 2.5 mg twice daily and aspirin provides some vascular benefits (including on stroke) *even in the absence of associated AF*, but at the risk of more major bleedings.

Any combination of therapeutic OAC and antiplatelets increases the risk of major bleeding and intracranial hemorrhage. In the COMPASS trial,[18] combination therapy (even using low-dose rivaroxaban, lower than the dose used for stroke prevention in AF) increased major bleeding overall, but not intracranial bleeds or fatal bleeds. Proactive mitigation of bleeding risks should be directed at the modifiable bleeding risk factors (uncontrolled blood pressure, reducing alcohol excess, etc.) and scheduling the high bleeding risk patients for early review and follow-up. In a prospective cluster randomized trial of general AF patients, this resulted in a reduction in major bleeding at 1-year follow-up and an increase in OAC use.[7]

Better Functional and Psychological Status

Improved functional and psychological status is a goal of holistic poststroke care, and this involves a multidisciplinary approach with rehabilitation and allied health care professionals. The majority of stroke patients finally achieve a degree of functional independence in their daily living, which is inversely related to the severity of stroke. Limited limb movement is not the only reason for functional dependence: other contributors include ataxia, aphasia, cognitive defects, poor coordination of movement, sensory defects, and others. There are several prognostic tools to predict functional status after stroke.[19–22] The modified Rankin scale, a 7-level, clinician-reported, measure of global disability, is the most widely employed outcome scale in stroke medicine and research.[23]

Stroke survivors who achieve greater functional gain during inpatient rehabilitation had better health-related quality of life and were more likely to be independent at follow-up.[24]

Poststroke depression (PSD) constitutes an essential complication of stroke and is associated with unfavorable outcomes after stroke. Approximately one-third of stroke survivors will develop PSD at some point, with the frequency being higher at the first year after stroke and then declining. The severity of PSD is related to unfavorable outcome.[25] The main factors contributing to PSD are physical disability, stroke severity, history of depression, and cognitive impairment.[26]

Poststroke dementia is another major but underrecognized complication poststroke. Its prevalence is approximately 30% among stroke survivors and its incidence rises gradually through the myocardial infarction, epileptic seizures, years after a stroke. Older age, low education status, dependence on others for daily living, prestroke cognitive decline without dementia, diabetes mellitus, AF, and other cardiac arrhythmias, sepsis, congestive heart failure, silent infarcts, brain atrophy, and leukoaraiosis are contributors of poststroke dementia. Given the close link between stroke and dementia, a practical clinical approach is needed, and neuropsychological evaluation should be adapted to the clinical status.[27,28]

Cardiovascular Risk Factors and Comorbidity Optimization (Including Lifestyle Changes)

Unsurprisingly, many stroke patients have multiple comorbidities, and part of integrated care is to address risk factors in a holistic manner—management of AF, atherosclerosis, arterial hypertension, heart failure, diabetes mellitus, dyslipidemia, sleep apnea, and underlying cardiac ischemia—with the aim of reducing the cardiovascular risk burden in these patients.

Blood pressure lowering has a major impact on major cardiovascular events, including stroke.[29] In the Blood Pressure Lowering Treatment Trialists' Collaboration, a 5 mm Hg reduction of systolic blood pressure reduced the risk of major cardiovascular events by approximately 10%, irrespective of previous diagnoses of cardiovascular disease (CVD), and even at normal or high-normal blood pressure values.[29] Thus, a fixed degree of pharmacological blood pressure lowering is similarly effective for primary and secondary prevention of major CVD, even at blood pressure levels currently not considered for treatment. This emphasizes the importance on reducing cardiovascular risk rather than focusing on blood pressure reduction itself.

Obstructive sleep apnea (OSA) is prevalent in stroke patients, and has been related to stroke severity,[30] but OSA is also associated with many stroke risk factors, such as AF and hypertension. Obesity is associated with increased CVD risk, including a predisposition to incident AF, as does excess alcohol or stimulant use. Heavy alcohol consumption predisposes to both hemorrhagic and nonhemorrhagic stroke,[31] as does smoking whereby the risk of stroke is increased by 12% for each increment of five cigarettes per day.[32] Therefore, lifestyle changes can help. Indeed, a scientific statement from the American Heart Association promoted "Life's Simple 7," to address modifiable risk factors for cognitive decline, including depression, hypertension, physical inactivity, diabetes, obesity, dyslipidemia, poor diet, smoking, social isolation, excessive alcohol use, sleep disorders, and hearing loss.[33] These risk factors can be routinely identified and managed by primary care clinicians, especially with patient engagement and empowerment. Additional education and counseling can also improve a patient's understanding, and adherence and compliance to treatments.[9,10]

Conflict of Interest
None declared.

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