

Global voices on atrial fibrillation: South/Southeast Asia



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Atrial fibrillation (AF) is a leading cause of mortality and morbidity worldwide.^{1,2} Despite the improvement in the rate of oral anticoagulant (OAC) use for stroke prevention, the residual risk of remain high.^{3,4} It is recommended that AF patients require a holistic care approach (ie, ABC [Atrial Fibrillation Better Care] pathway) to improve the outcomes.^{5–7}

In this article, we summarize AF management issues in South and Southeast Asia. The first part refers to the scenario from Thailand, from the COOL-AF (COhort of antithrombotic use and Optimal INR Level in patients with nonvalvular atrial fibrillation in Thailand) registry, which is the most extensive exploration of AF in Thailand and, probably, Southeast Asia. Conduct of a clinical trial to improve warfarin management in Thailand is also described. Subsequent parts refer to highlighting rural challenges in AF care in India [and the KERALA-AF (Kerala Atrial Fibrillation) registry, a large comprehensive AF registry in South Asia]—and in Sri Lanka, we focus on mapping patient pathways and community engagement to enhance AF awareness, etc.

Atrial fibrillation management in Thailand: Lessons learned from the COOL-AF registry

The inspiration to have an AF registry in Thailand was coming from the practice of using warfarin as the main OAC in

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KEY FINDINGS

- Atrial fibrillation is a major burden in the Asian population, leading to an increased risk of adverse clinical outcomes.
- Major bleeding is more common in Asians compared with non-Asians, especially when warfarin is used.
- There are many areas of suboptimal atrial fibrillation management including the low rate of non-vitamin K antagonist oral anticoagulant use, low time in the therapeutic range with warfarin, and low compliance to the ABC (Atrial Fibrillation Better Care) pathway.
- Because widespread adoption of direct oral anticoagulants will not occur immediately, implementation of the ABC pathway, specialized multidisciplinary care, and patient education is essential.

Thailand, and we often see the bleeding complication relating to warfarin.⁸ We noticed that there was a report showing that intracranial bleeding (ICH) rate in Asian population was greater than non-Asians.⁹ The COOL-AF registry was the initiation from cardiologists interested in AF. The registry was financially supported by Health Systems Research Institute and the Heart Association of Thailand. The COOL-AF registry involved 27 hospitals distributed in all regions in Thailand; approximately half were university hospitals. There were a total of 3461 nonvalvular AF patients enrolled during 2014 to 2017. The original aims of the registry were to determine the optimal international normalized ratio (INR) levels in patients who used warfarin, to study the

antithrombotic patterns, and clinical outcomes. Patients were followed up every 6 months until 3 years. The clinical outcomes were death, ischemic stroke/systemic embolism (SSE), major bleeding including ICH, and heart failure.¹⁰

The key findings from the results of the COOL-AF registry were as follows:

1. The overall rate of OAC use was 75.3%; it was 81.6% in high-risk groups.¹⁰ Non-vitamin K antagonist OACs (NOACs) were used in 9.1% of patients who were on OAC.
2. The incidence rates of death, SSE, major bleeding, ICH, and heart failure were 4.21, 1.51, 2.25, 0.78, and 2.84 per 100 person-years, respectively.¹¹
3. The use of NOACs was associated with a reduction in the rate of SSE, and major bleeding including ICH.
4. Among patients who were on warfarin, time in the therapeutic range (TTR), which is the key measure of OAC control, is the major determinant for clinical outcome. Patients with a TTR >65% had a better outcome than those with a TTR <65%.¹² However, only one-third of warfarin patients had a TTR >65%.
5. The treatment compliant to the practice guideline for OAC management was associated with a better outcome.¹³
6. Management that was adherent to the ABC pathway, which reflects holistic or integrated care management, had better outcomes compared with those that were non-adherent to the ABC pathway.¹⁴

The ABC pathway applies to not only the appropriate use of OACs, but also symptom management and the treatment of cardiovascular risk factors and comorbidity.¹⁵ Implementation of the ABC strategy should have greater focus in the Asian population because it impacts on clinical outcomes, especially as warfarin remains the major OAC in many Asian countries. Even in well-resourced settings like the United States, Hylek and colleagues¹⁶ highlighted the importance of maintaining therapeutic levels of warfarin and the limited tolerability. Despite a trend toward the increased use of NOACs in the Asian population, these drugs still remain costly, and generic versions are only slowly becoming more accessible in developing countries. Hence, warfarin is expected to remain predominant for some time in those areas.

Thus, a coordinated approach that includes specialized care, patient education, and technology-enhanced monitoring of anticoagulation therapy, such as INR and medication adherence, is essential. Moreover, it is imperative that governments recognize the seriousness of AF and allocate sufficient funds to support these initiatives.

The results of the COOL-AF registry led to the next step of data collection in the COOL-AF phase 2 registry. The main aims of phase 2 registry were to study the changes in antithrombotic pattern and the association with clinical outcomes. Moreover, the COOL-AF phase 2 registry also has additional aims: (1) to validate the predictive model for clinical outcomes developed from the phase 1 data, (2) to determine the rate of off-label NOAC dosing and the effect on outcomes, and (3) to collect frailty data and its impact on out-

comes. We also have a plan to study the management pattern in hospitals in rural region in Thailand. There have been several issues on AF management in rural regions such as the availability of medications, as well as blood tests, socioeconomic status and health insurance issues, and the associated understanding of disease management and AF-related complications.

We hope that the COOL-AF phase 2 registry and the data on AF management in rural areas will shed more light for a better understanding of the treatment gaps in Thailand and will lead to a better care of AF patients. [Figure 1](#) shows the interactions of healthcare personnel and AF patients in a rural Thai hospital setting.

Improving warfarin management for Thai AF patients

The increasing prevalence of AF globally, including in Thailand, presents a growing healthcare challenge due to associated risks like stroke and heart failure. OACs with vitamin K antagonists (ie, warfarin) or NOACs are crucial for stroke prevention. While NOACs offer several advantages over vitamin K antagonists and are the preferred OAC for eligible AF patients, their accessibility is constrained in low-to-middle income countries (LMICs). Nevertheless, warfarin is frequently managed suboptimally, resulting in an increased risk of thromboembolism, major bleeding, and mortality.¹² Improving the management of warfarin is essential to enhance outcomes for AF patients and reduce healthcare costs. Factors influencing the effectiveness of warfarin, such as medication adherence and drug interactions, must be addressed.

The TREAT (TRIAL of an Educational intervention on patients' knowledge of Atrial fibrillation and anticoagulant therapy, INR control, and outcome of Treatment with warfarin) intervention was developed through the integration of theoretical and clinical frameworks, as well as patient input. This comprehensive behavior modification package includes an educational booklet, diary, worksheet, and reinforcement DVD. The booklet delves into AF etiology, warfarin pharmacokinetics, stroke and bleeding risks during treatment, and lifestyle modifications (diet, alcohol, and behavior). The DVD features narratives from healthcare professionals and expert patients, covering AF pathology, consequences, treatment modalities, warfarin therapy, INR monitoring, lifestyle changes, and common barriers to anticoagulation adherence. Worksheets facilitate self-assessment of stroke risk (CHA₂DS₂-VASc [congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65-74 years, sex category] score), identification of personal barriers to warfarin adherence, and establishment of individualized lifestyle goals. Additionally, a self-monitoring diary tracks dietary habits, alcohol consumption (in units), warfarin regimen, and INR values. To mitigate language barriers, the intervention underwent cultural adaptation and translation into Thai, following



Figure 1 A: Warfarin education for individual patients in rural hospital by healthcare personnel. B. Group education for atrial fibrillation complication and management in a rural hospital in Thailand.

forward and backward translation by bilingual experts. A trial of the Thai version among AF patients with varying levels of education and age was conducted, incorporating patient feedback to optimize the usability of the intervention. The TREAT study demonstrated that a single educational-behavioral intervention (TREAT intervention) for warfarin in AF patients notably enhanced TTR at 6 months compared with standard care alone.^{17,18} However, implementing such interventions universally for all AF patients on warfarin may not be feasible. Identifying patients less likely to achieve optimal INR control and delivering a structured educational-behavioral intervention as needed could offer a practical and cost-effective management strategy. The SAME-TT2R2 score, which includes demographic and clinical variables has developed to identify likelihood of achieving suboptimal TTR in patients with a score ≥ 2 .

Therefore, the TREATS-AF (a prospective randomized trial examining the impact of an educational intervention vs usual care on anticoagulation therapy control based on a SAME-TT2 R2 score-guided strategy in anticoagulant-naïve Thai patients with atrial fibrillation) study¹⁷ was conducted and aimed to evaluate whether employing a SAME-TT2R2 score-guided strategy alongside the TREAT intervention, in addition to standard care, could enhance anticoagulation control with warfarin (assessed by percentage TTR) over a 12-month period, compared with standard care alone. It was a multicenter, open-label, parallel-group, randomized controlled trial conducted in Thailand involving adult patients (≥ 18 years of age) with AF who have not been treated with anticoagulants. Participants were randomly assigned to 1 of 2 groups: those receiving a SAME-TT2R2 score-guided strategy with educational intervention in addition to usual care vs those receiving usual care alone. The planned duration of follow-up was 12 months. The primary outcome measure was the TTR at 12 months. Secondary outcomes included TTR at 6 months; incidences of thromboembolic

and bleeding events at 12 months; composite major adverse cardiovascular events at 12 months; changes in patients' AF-related knowledge from baseline to 6 months and 12 months; cost-effectiveness; quality of life assessed at baseline, 6 months, and 12 months using the EQ-5D-5L (Thai version); and patient satisfaction and perceptions of the TREAT intervention. Additionally, a qualitative study will be conducted to explore patient perceptions of the TREAT intervention.

Rural population challenges in relation to access to care and electrophysiology services: Insights from India

Nearly 80% of global cardiovascular diseases (CVDs) occur in LMICs.¹⁹ The incidence of cardiovascular death is higher in low-income countries, even though such countries have lower risk factors, and rural communities have higher fatality rates than their urban counterparts despite their lower risk factors.²⁰ In India, CVD remained the leading cause of death and was responsible for 31.6% of total deaths in the year 2017.²¹ The prevalence of CVD in India has more than doubled, from 25.7 million in 1990 to 54.5 million in 2016.²² Indian patients with CVD are a decade younger than their European counterparts, and the majority (62%) of all cardiovascular deaths in India are premature.²³

In India, 65% of people live in rural areas,²⁴ but cardiac centers that have the state-of-the-art infrastructure for providing specialized care for AF patients are concentrated in tier 1 cities and are nearly absent in smaller towns and rural areas. There are significant urban-rural differences in the care for AF patients in India. Three key elements drive the quality of care patients with AF receive in rural India: insufficient access to appropriate modalities for AF diagnosis, limitations in the knowledge and practices of primary healthcare providers involved in the care of these patients, and inadequate adherence to prescribed therapy.

Data on Indian AF patients are available mainly through 2 large Indian hospital-based registries, the IHRS-AF (the Indian Heart Rhythm Society-Atrial Fibrillation) nationwide registry, which recruited patients from 24 specialized centers located in urban areas during 2011 to 2012,²⁵ and the regional KERALA-AF registry,^{26–28} which recruited 3421 patients from 53 hospitals across the state of Kerala from both urban and rural areas during 2016 and 2017. Unlike other states in India, the urban-rural difference in Kerala is not prominent. Kerala is one of the most urbanized states in India with settlements in the rural-urban continuum pattern, with a higher affinity toward urbanization.²⁹ Primary health centers, under the aegis of the National Rural Health Programme, cater to the majority of the healthcare needs of the rural population of India. When feasibility limits the provision of dedicated cardiologists at such sites,³⁰ training of semi-skilled frontline health workers has been demonstrated to be useful in population screening for cardiovascular risk factors.^{31,32}

A comprehensive approach addressing various challenges faced by the rural population is required to reduce the urban-rural difference in care for AF patients in India.

Some of the major challenges that rural AF patients face in India are as follows:

1. Access to healthcare services: There is an urgent need to expand the availability of cardiac care services in rural areas. The health systems and healthcare facilities in rural areas need to implement programs focusing on AF diagnosis, management, and follow-up.
2. Training the healthcare providers in rural areas to detect and manage AF, including appropriate use of anticoagulation therapy and referral of patients who require specialized care.
3. Offering specialized training programs for healthcare professionals in rural areas on interpreting electrocardiograms and patient counseling.
4. The need to enhance awareness and education of AF among the rural population on its symptoms, risk factors, and the significance of seeking timely medical attention.
5. An integrated care model can be established that involves collaboration between the primary health centers in rural areas with cardiologists in specialized centers in urban areas to deliver comprehensive AF management like rate or rhythm control, stroke prevention, risk factor modification, etc.
6. Making essential medication for AF treatment such as anticoagulants and rate/rhythm control drugs accessible and affordable to patients.
7. Promoting telemedicine and mobile health solutions: Telemedicine services can be extended to rural areas, allowing patients to consult with cardiologists remotely. The use of mobile health platforms to deliver educational health resources, monitor patients remotely, and distribute medication reminders to rural patients can be encouraged to bridge the gap between urban and rural AF patients.
8. A dedicated program for training and equipping frontline health workers for the appropriate diagnosis and timely referral of patients with newly diagnosed AF could be

the cornerstone for establishing quality rural healthcare for atrial fibrillation.

9. Conduct surveillance programs to better understand the burden of AF in rural populations to identify disparities in care delivery and outcomes and inform policymakers for equitable resource allocation.

By implementing these strategies, India can work toward reducing the urban-rural difference in the care of AF patients and can improve overall outcomes.

Streaming the comprehensive management of atrial fibrillation in South Asian LMICs: Patient pathway insights from a Sri Lanka

AF is a prevalent cardiac arrhythmia, impacting millions globally, with a projected increase in prevalence.³³ It poses a significant health burden due to its association with cardiovascular events and heightened stroke risk.³⁴ Established clinical strategies like the ABC pathway emphasize comprehensive management approaches to mitigate AF-related complications.^{15,35} The underestimation of AF prevalence in LMICs underscores the need for improved awareness and access to diagnostics.^{36,37} Implementing established care pathways and enhancing healthcare infrastructure can mitigate this burden and improve patient outcomes.³⁸

Sri Lanka, a South Asian LMIC with a population of 22 million, has a well-established government-led centralized national health service.³⁹ Sri Lanka faces challenges in addressing the rising burden of CVDs, necessitating improved AF awareness and management integration despite available healthcare infrastructure and technology. Our work aimed to deepen our understanding of AF, enhance awareness of AF, and improve the management pathway, ultimately enhancing patient care (Figure 2). Community engagement and involvement has raised awareness and engaged local communities to the burden of AF and AF-related stroke (Figure 2).^{40,41}

This mixed methods approach facilitated a comprehensive evaluation of AF prevalence and associated factors, enhancing the understanding necessary for effective care planning and implementation.⁴² Our pathway mapping study identified inefficiencies in referral, diagnosis, and ongoing management.⁴³ Delays in accessing care and ongoing management were health-seeking behaviors and atomistic healthcare structures. Our published pathway mapping and handover work in Sri Lanka revealed inefficiencies in referral, diagnosis, and ongoing AF management.⁴³ We showed that clinical handover between providers of care and empowered patients is critical for continuity of care in such chronic disease management, without which patient safety is at risk and health outcomes are compromised. Improving public health literacy regarding AF and building patient autonomy while understanding the importance of their daily lifestyle behaviors and family involvement may be advantageous in counteracting the inefficiencies in the current AF care pathway in Sri Lanka.



Figure 2 National Institute for Health and Care Research Global Atrial Fibrillation project: existing care evaluation of atrial fibrillation and improve it via capacity development and digitally integrated interventions in Sri Lanka.

Conclusion

Based on the available data in South and Southeast Asia, there are several issues for AF management improvement. Example of the key concerns were that (1) AF in South and Southeast Asia had a high mortality rate and high risk of complication, especially major bleeding; (2) the majority of AF patients use warfarin for stroke prevention; (3) the rate of optimal time in therapeutic range is low; and (4) the

management of comorbidities remains suboptimal. Future directions to reduce the risk of AF patients in this region should be the immediate act, which includes not only the attempts to give appropriate treatment to the patients, but also raising the concern to policymakers to make the appropriate drugs, such as NOACs, available for the patients and delivering education to the population at risk, population in general, and family members.

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