Clinical Epidemiology

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EDITORIAL

Stroke in Heart Failure

This article was published in the following Dove Press journal:
Clinical Epidemiology

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Hippocrates, the father of medicine, first recognised stroke 2400 years ago after noting that occlusion of the carotid arteries caused loss of consciousness.[1] In the twenty-first century, stroke is ranked as the second leading cause of death with an estimated mortality of around 5.5 million in 2016.[2] Additionally, over 50% of stroke survivors suffer chronic disability.[3] Heart failure (HF) is a global cause of morbidity and mortality with an estimated 40 million cases in 2015.[4] Long-term multi-system complications of HF (Figure 1) and multimorbid disease interactions are of increasing importance and demand a multidisciplinary approach. The prevalence of both stroke and HF is expected to increase due to an ageing population.[5,6] It has thus far proven difficult to elucidate the strength of the association between HF and stroke. This is due to the presence of many confounding factors in previous studies including but not limited to small sample sizes, heterogeneous study cohorts, differing definitions of stroke, multiple confounding factors and a short duration of follow up.[7–12] The Framingham Study showed that HF was associated with a two to three times higher risk of stroke.[13] However, patients with HF also have several co-morbidities which on their own have a propensity to cause ischaemic stroke, such as atrial fibrillation (AF), hypertension, ischaemic heart disease and diabetes.[8,14] Lip et al, demonstrated that patients without AF or prior stroke in the study had a hazard ratio of 2.3 (95% Confidence interval (CI) 1.8–3.0) for ischemic stroke in patients with vs without incident heart failure.[8] Abdul-Rahim et al reported that a clinical trial population of patients with HF with AF had a higher average annual incidence rate of stroke compared with patients with HF and without AF (1.6% vs 1.2%).[15]

The presumed aetiology of stroke in HF is likely to be secondary to augmentation of the Virchow's triad: prothrombotic factors, endothelial injury and left ventricular thrombus formation with subsequent cerebral embolism.[16,17] These vascular alterations are observed in both HF with reduced ejection fraction (HFrEF) as well as in HF with preserved ejection fraction (HFpEF). Prognostically, patients who suffer stroke and have HF as an existing comorbidity appear to have much greater rates of mortality. In this case, HF appears to add insult to injury.[18,19]

There have been several attempts to quantify the risk of stroke in HF with mixed results. A 2015 study looking at the CHA_2DS_2-VASc scoring system (a validated tool for AF patients) found that whilst the scoring system had a modest predictive accuracy in this cohort, the clinical utility itself was yet unclear.[20] More recent data from a 2017 retrospective study has suggested that the CHA_2DS_2-VASc scoring system has similar validity in both an AF and a non-AF HF cohort of patients.9 The

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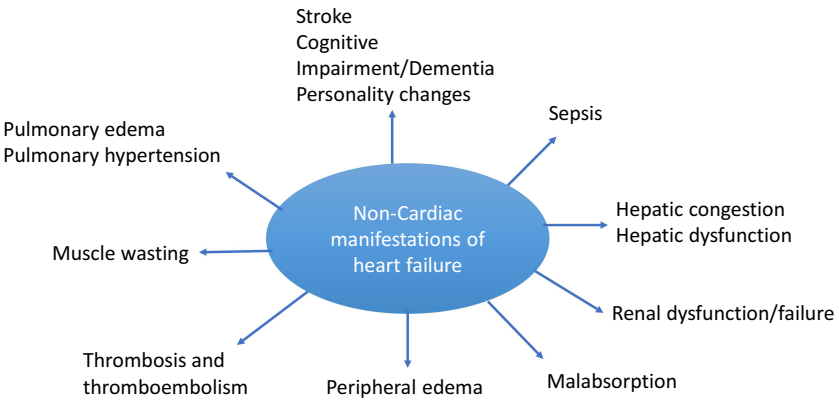

Figure 1 Non-cardiac complications of heart failure.

prevention of stroke in this cohort is also unclear, with data from a meta-analysis of 4 randomized control trials with a total of 3681 patients comparing warfarin to aspirin demonstrating no difference in mortality. However, warfarin conferred a lower stroke risk at the cost of a higher bleeding risk.[21]

In this issue, Tai and colleagues attempt to shed further light on the topic of the long-term risk of stroke and poststroke adverse outcomes in a HF population. There were 2 separate datasets studied:

1. Study 1–20,072 adults aged ≥30 years newly diagnosed with HF extracted from the Taiwan national health insurance programme between 2000 and 2005. This group was compared against a cohort of 80,288 non-HF patients matched based on age and sex. Both groups had no history of stroke.
2. Study 2–480,604 adults aged ≥30 hospitalized for stroke with and without HF between 2002 and 2009. In this cohort were 30,532 patients with a prior diagnosis of HF.

From their analysis, several important points of discussion emerge in study 1. Firstly, in the HF cohort, stroke risk was significantly higher (hazard ratio (HR) 2.32, 95% CI 2.21–2.43). Secondly, this increased risk of stroke was independent of age and medical background. Thirdly, the association between increased stroke risk was seen throughout the follow-up period when patients who developed stroke in the first 12 months (HR 1.72, 95% CI 1.63–1.81) after the onset of HF were excluded. In study 2, the main finding is that in the HF cohort there was a higher risk of poststroke pneumonia (Odds ratio (OR) 1.31, 95% CI 1.24–1.38), sepsis (OR 1.25, 95% CI 1.17–1.35), intensive care admission (OR 1.47, 95% CI 1.41–1.54), and overall mortality during the hospitalisation (OR 1.44, 95% CI 1.31–1.59).

Tai et al's study benefits from a large sample size and long duration of follow-up lending credible evidence to two emerging consensuses. Mainly, that HF is a strong risk factor for stroke and that stroke with underlying HF is much worse prognostically. The results reported are consistent with multiple previous studies.[7–11] Furthermore, this study demonstrates that stroke risk persists and does not normalise after 6 months, a finding that has previously been shown.[8] Several limitations, most of which are acknowledged by the authors, must be considered when interpreting this data. First, this is a retrospective observational study and therefore open to unknown confounding factors which may explain these findings; second, misclassification is common in data that relies on coding for diagnosis; third, the population studied is a mainly homogenous Taiwanese population, therefore these findings may not necessarily be replicated in other ethnicities.

In conclusion, the researchers' findings highlight the complex nature of the link between HF and stroke and its negative prognostic implications, reflecting earlier study results and solidifying this link. Going forward, important future areas that need to be researched include 1) identification and validation of an appropriate scoring system for stroke risk in HF to highlight low and high-risk patients, and 2) identification of appropriate prophylactic treatment to help reduce the stroke burden in this cohort.

Disclosure

Professor Lip reports consultancy and speaker fees from Bayer, Bayer/Janssen, BMS/Pfizer, Biotronik, Medtronic, Boehringer Ingelheim, Microlife, Roche,

and Daiichi-Sankyo outside the submitted work. Dr Sankaranarayanan reports speaker fees from Novartis, Astra Zeneca, Vyfor, BMS/Pfizer and research grants from Biotronik UK, British Heart Foundation outside the submitted work. The authors report no other conflicts of interest in this work.

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