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Left atrial appendage occlusion is promising, not concerning

Kasper Korsholm[1], MD; Jens Erik Nielsen-Kudsk[1]*, MD, DMSc

Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark

We appreciate the interest of Dr Stöllberger and Dr Schneider in our recent study on aspirin monotherapy after left atrial appendage occlusion (LAAO) in a high bleeding risk population[1]. The authors share their concerns about LAAO, in particular focusing on mortality. In the following, we will try to reply to their questions and comments.

In our study cohort, 20 patients died during follow-up (266 patient-years; 7.5/100 patient-years). The median time from LAAO to death was 403 days (IQR: 251-1,093). The cause of death was infection (n=6), aortic stenosis (n=3), heart failure (n=2), cancer (n=2), renal failure (n=2), intracranial bleeding (n=1), traumatic thoracic bleeding (n=1), major gastrointestinal bleeding (n=1), ischaemic stroke (n=1), and one unexplained death in a 93-year-old patient.

As highlighted by Dr Stöllberger and colleague, the mortality rate was higher compared to the PROTECT-AF, ASAP, and ACP studies. Novel results from the EWOLUTION registry report 6.9 deaths/100 patient-years[2], and the Iberian LAAO registry reported 5.8 deaths/100 patient-years[3]; both report CHA_2DS_2-VASc scores similar to the aforementioned studies. However, $CHADS_2$ and CHA_2DS_2-VASc scores help to predict the stroke risk[4]. A wider range of risk factors and comorbidities than those summarised in the CHA_2DS_2-VASc score must be taken into account when comparing mortality rates. The mean HAS-BLED score in our study was 4.1, and was the highest among the mentioned studies (2.3-4.1). Though it is not reported explicitly, the lowest HAS-BLED score is expected in the PROTECT-AF trial, since this was based on warfarin eligible patients[5]. Other variations in baseline characteristics and comorbidities may affect mortality. For example, previous intracranial haemorrhage (ICH) was the primary indication for LAAO in 45% of our cohort. All-cause mortality for these patients ranges between 9.7 and 19.5 deaths/100 patient-years, depending on the post-ICH antithrombotic regimen[6]. In a recently published propensity score-matched study, LAAO was suggested to have major benefit over standard medical care in patients with AF and previous ICH[7]. Patients treated by LAAO had a significantly lower risk of the primary composite outcome of mortality, ischaemic stroke and major bleeding as compared to standard

*Corresponding author: Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, DK-8200 Aarhus N, Denmark. E-mail: je.nielsen.kudsk@gmail.com

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medical therapy (hazard ratio 0.16 [0.07-0.37]). In addition, the separate risk of all-cause mortality was significantly reduced by LAAO (hazard ratio 0.11 [0.03-0.51]).

We agree with the authors that atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) levels might be altered in relation to LAA elimination. However, clinical data after LAA ligation with the LARIAT® device (SentreHEART, Inc., Redwood City, CA, USA) suggest that neuroendocrine homeostasis is restored after four months[8]. No change in sodium, potassium, glucose or glomerular filtration rate was observed after four months[8]. Only systolic blood pressure was reduced, which may even be beneficial, since 82% had a diagnosis of hypertension at baseline.

At follow-up in our LAAO aspirin monotherapy cohort, 81% had complete sealing, 12% had 1-3 mm peri-device leak and 6% had 3-5 mm leak, while 1% had >5 mm leak. Studies have not found any association between peri-device leaks after transcatheter LAAO and increased risk of thromboembolism[9,10].

In conclusion, mortality may not easily be compared across studies based solely on CHA_2DS_2-VASc scores. In turn, the neuroendocrine alterations after LAAO appear temporary, without any data indicating a sustained negative effect on glucose or electrolyte homeostasis, while they might have a beneficial effect on hypertension. Thus, transcatheter LAAO, as a new therapy, is promising for stroke prevention in patients with atrial fibrillation and high bleeding risk, not concerning.

Conflict of interest statement

J.E. Nielsen-Kudsk is a proctor for St. Jude Medical/Abbott. The other author has no conflicts of interest to declare.

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