Over the past fifteen years many researchers have been engaged in deciphering the interrela- tionship between migraine and patent foramen ovale (PFO). Available studies suggest a bi-directional relationship between migraine, in particular migraine with aura, and PFO. The prevalence of PFO across several studies is 54% among migraineurs with aura compared to 24% among controls. Likewise, among patients with PFO 27% reported any migraine compared to 14% among those without PFO and 36% of patients with PFO reported migraine with aura compared to 13% among those without PFO. Additional studies reporting cessation or improvement of migraine in up to 88% of patients undergoing PFO closure for other reasons than migraine seem to lend further su t to a causal association between the two conditions. However, these studies suffered from major limitations.

1.) Data collection was retrospective, which is subject to recall bias.
2.) Most studies were of limited to small sample size.
3.) All studies lacked a control group and were performed in selected patients. Hence mi-graine improvement may be explained by a placebo effect, which is known to be high in migraine.
4.) Many patients were treated with aspirin and/or clopidogrel because of the implanted devices and these drugs are known to possess migraine preventive properties.
5.) It has been reported that migraine may not only subside after PFO closure in some pa-tients, but may also develop de novo in others, and many stroke patients suffering from co-morbid migraine experience an improvement of their headaches before PFO closure.

The results from the first clinical trial investigating the effects of PFO closure on migraine showed no efficacy of PFO closure. The MIST (Migraine Intervention with STARFlex Technology) trial was a prospective, multicenter, double-blind, sham-controlled trial. Of the 432 patients screened, 163 (38%) had moderate or large PFO. One-hundred-and-forty-seven patients were randomized to transcatheter PFO closure or sham procedure and followed for six months. The primary end point was migraine headache cessation. No significant differences were found between the implant and sham group. Serious adverse effects were more frequent in the implant group.

The Percutaneous Closure of PFO in Migraine with Aura (PRIMA) trial was a multicentre, randomized trial to investigate the effect of percutaneous PFO closure in patients refractory to medical treatment. Migraine with aura patients and PFO who were unresponsive to preventive medications were randomized to PFO closure or medical treatment. Both groups were given acetylsalicylic acid 75-100 mg/day for 6 months and clopidogrel 75 mg/day for 3 months. The primary endpoint was reduction in monthly migraine days during months 9-12 after randomization compared with a 3-month baseline phase before randomization. 107 patients were randomly allocated to treatment with an Amplatzer PFO Occluder (N = 53) or control with medical management (N = 54). Eighty-three patients (40 occluder, 43 control) completed 12-month follow-up. Mean migraine days at baseline were 8 (+/-4.7 SD) in the closure group and 8.3 (+/-2.4) in controls. The primary endpoint was negative with -2.9 days after PFO closure vs. -1.7 days in control group (P = 0.17). Patent foramen ovale closure caused five adverse events without permanent sequelae. In summar y we have 2 clearly negative randomised trials.

In conclusion, there is insufficient evidence to support a causal link between PFO and mi-graine with aura and a PFO closure cannot be recommend as a treatment option for either migraine with or without aura.

At the conclusion of this presentation, attendees should be better able to:

- Understand that PFO closure is no option for the prevention of migraine with aura
- Prevent patients to see an interventional cardiologist
- Understand the impact of the MIST and PRIMA trial
- Learn about the epidemiology of PFO and migraine
- Avoid bias in patient selection