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► To cite this version:

Noelie Miton, François Godart, Guiti Milani, Zakaria Jalal, Clément Karsenty, et al.. Patent foramen ovale closure in children without cardiopathy: Child-PFO study. Archives of cardiovascular diseases, 2020, 113 (8-9), pp.513-524. 10.1016/j.acvd.2020.03.021 . hal-04526882

HAL Id: hal-04526882

<https://hal.science/hal-04526882v1>

Submitted on 29 Nov 2024

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Patent foramen ovale closure in children without cardiopathy: Child-PFO study

Fermeture du foramen ovale perméable chez l'enfant sans cardiopathie ; étude FOP-pédia

Abbreviated title: PFO closure in children without cardiopathy

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Summary

Background. – Closure of patent foramen ovale is well-managed in adults, but is performed less frequently in children.

Aim. – To analyse all patent foramen ovale closures performed in the past 20 years in French paediatric centres.

Methods. – Retrospective study of patent foramen ovale closures in children without cardiopathy in nine centres between 2000 and 2019.

Results. – Forty-one procedures were carried out in children (median age: 14.9 years). Thirty-one patent foramen ovals were closed after a transient ischaemic attack or stroke, six for a left-to-right shunt and four for other reasons. Transthoracic echocardiography was used for 72.2% of the diagnoses and transoesophageal echocardiography for 27.8%. A substantial degree of shunting was found in 42.9% of patients and an atrial septal aneurysm in 56.2%. General anaesthesia with transoesophageal echocardiography guidance was performed in 68.3% of the procedures; local anaesthesia and transthoracic echocardiography or intracardiac echocardiography was performed in 31.7%. The success rate was 100%. The median fluoroscopy time was 4.14 minutes: 3.55 minutes with transoesophageal echocardiography; and 4.38 minutes with transthoracic echocardiography ($P=0.67$). There was only one periprocedural complication (2.4%). Postoperatively, 80.5% of patients were treated with aspirin and 12.2% with an anticoagulant. The rate of complete occlusion was 56.8% immediately after the procedure, 68.6% at 1 year and 92.3% at the last follow-up. There were no delayed complications or cases of recurrent stroke during follow-up (median follow-up: 568 days).

Conclusion. – Closure of patent foramen ovale in children appears to be safe and effective, as we noted a low rate of immediate complications, no delayed complications and no stroke recurrence in this indication.

Résumé

Contexte. – La fermeture du foramen ovale perméable (FOP) est bien maîtrisée chez l'adulte, mais est moins fréquente chez l'enfant.

Objectif. – Analyser toutes les fermetures de FOP au cours des 20 dernières années dans les centres de cardiologie interventionnelle pédiatriques français.

Méthodes. – Étude rétrospective de la fermeture du FOP chez l'enfant sans cardiopathie dans 9 centres de 2000 à 2019.

Résultats. – Quarante et une procédures ont été réalisées chez l'enfant (âge médian de 14,9 ans). Trente et un FOP ont été fermés pour un accident ischémique neurologique transitoire (AIT) ou constitué (AVC), 6 pour un shunt gauche-droit et 4 pour une autre cause. Le diagnostic a été fait par échocardiographie transthoracique (ETT) dans 72,2 % des cas, et échographie transoesophagienne (ETO) dans 27,8 % des cas. 42,9 % des patients avaient un shunt important, et 56,2 % un anévrisme du septum inter-atrial (ASIA). 68,3 % des procédures ont été réalisées sous anesthésie générale, guidée par ETO et 31,7 % sous anesthésie locale, guidée par ETT ou échographie intracardiaque (EIC). Le taux de succès était de 100 %. La durée médiane de scopie était de 4,14 minutes : 3,55 avec ETO, 4,38 avec ETT ($P = 0,67$). Il y a eu une seule complication per-procédure (2,4 %). En post-procédure, 80,5 % des patients ont été traités par aspirine et 12,2 % par anticoagulant. Le taux d'occlusion complète était de 56,8 % immédiatement après la procédure, de 68,6 % à 1 an et de 92,3 % lors du dernier contrôle. Il n'y a pas eu de complication tardive, ni de récurrence d'AVC au cours du suivi (suivi médian de 568 jours).

Conclusion. – La fermeture du FOP chez l'enfant est une procédure sûre et efficace, avec un faible taux de complications immédiates, aucune complication durant le suivi, ni de récurrence d'accident ischémique neurologique dans cette indication.

KEYWORDS

Patent foramen ovale;

Percutaneous closure;

Stroke

MOTS CLÉS

Foramen ovale perméable ;

Fermeture percutanée ;

Accident vasculaire cérébral

Abbreviations: ASA, atrial septal aneurysm; AVB, atrioventricular block; c-TTE, transthoracic echocardiography with contrast agent; FCPC, Paediatric and Congenital Cardiology Subsidiary of the French Society of Cardiology (Filiale de Cardiologie Pédiatrique et Congénitale); PFO, patent foramen ovale; TOE, transoesophageal echocardiography; TIA, transient ischaemic attack; TTE, transthoracic echocardiography.

Background

Nowadays, the closure of patent foramen ovale (PFO) in adults is a well-managed technique. Guidelines were published in 2018 and in 2019 [1, 2], based on large prospective studies after cryptogenic stroke [3-5]. However, experience with this technique in children and literature regarding PFO closure in children are much less substantial [6], and specific guidelines for this population have not yet been devised. In this study, we report on experience with PFO closure in children over the last 20 years at centres of paediatric interventional catheterization in France.

Methods

This was a retrospective study of cases of PFO closure in children without cardiopathy at centres of interventional catheterization in France since 2000. Fourteen centres from the French Congenital Catheterization Group of the Paediatric and Congenital Cardiology Subsidiary of the French Society of Cardiology (Filiale de Cardiologie Pédiatrique et Congénitale; FCPC) were contacted by e-mail to identify all cases of percutaneous PFO closure in patients aged < 18 years since 2000, and to establish the PFO treatment modalities at these various centres.

Each investigator at the participating centres completed an Excel spreadsheet to collect retrospectively all of the data necessary for the study. The collected data were processed and analysed by the two main investigators. Quantitative variables are expressed as medians (minimum–maximum) and categorical variables are expressed as numbers (percentages). All statistical analyses were carried out using the data that we were able to collect retrospectively. Chi-squared tests were used to calculate *P* values. *P* < 0.05 was considered statistically significant.

Results

The collected data covered the period from January 2000 to May 2019. Nine paediatric catheterization centres performing PFO closures in France took part in this retrospective study (Fig. 1 and Fig. 2).

Our study cohort comprised 41 patients: 25 girls (61%) and 16 boys (39%). Median age at the time of the procedure was 14.9 (3–17.8) years, median body weight was 52 (17–71) kg and median height was 160 (104–179) cm.

Indication for the closure

Thirty-one patients (75.6%) underwent PFO closure following a stroke or a transient ischaemic attack (TIA), six patients (14.6%) for a left-to-right shunt and four patients (9.8%) for other reasons: migraine ($n = 1$); cerebral abscess ($n = 2$); and before implantation of an endocavitary pacemaker for a high-grade atrioventricular block (AVB) ($n = 1$) (Fig. 3).

In the subgroup of pubescent patients ($n = 29$, 70.7%), defined *a posteriori* as being > 12 years of age, the indication was most often neurological: TIA or stroke ($n = 25$, 86.2%). For the prepubescent patients ($n = 12$, 29.3%), the indications were more varied: TIA or stroke ($n = 6$); cerebral abscess ($n = 2$); high-grade AVB requiring implantation of a pacemaker ($n = 1$); or a left-to-right shunt ($n = 3$) (Table 1).

In the “TIA/stroke” subgroup of patients, 26 (89.6%) had ischaemic signals on brain tomodensitometry or magnetic resonance imaging. Venous echo-Doppler of the lower limbs was carried out in 11 patients, and the results were positive for one. Seventeen patients were assessed by a neurocardiology team.

An element that would favour paradoxical embolism, according to the doctor’s evaluation, was identified for three patients: physical activity ($n = 1$); a theme park ($n = 1$); and coitus ($n = 1$). Risk factors for venous thromboembolic disease were found in three patients: pre-B acute lymphoblastic leukaemia ($n = 1$); association with oestrogenic contraception and tobacco use ($n = 2$). These factors promoting venous thromboembolic disease and paradoxical embolism were independent, and were only found in the pubescent patients. A thrombophilic assessment was carried out in 27 of the 31 patients from the “TIA/stroke” subgroup, and four were found to be positive: three heterozygous mutations of the *MTHFR* gene and one heterozygous mutation of the thrombin gene.

Diagnosis of PFO

The modality of diagnosis was known in 36 patients: it was made by transthoracic echocardiography (TTE) in 26 (72.2%) patients, and by transoesophageal echocardiography (TOE) in 10 (27.8%) (Fig. 4)

PFO anatomy (Fig. 5)

The anatomy of the PFOs is described in Table 2. This was difficult to assess retrospectively; indeed, the extent of the shunt was indicated in only 14 patients (34.1%), the size of the PFO in 13 (31.7%),

the presence of an atrial septal aneurysm (ASA) in 32 (78.1%) and the presence of a tunnel in 15 (36.6%). A substantial degree of shunting was found in 42.9% of patients, and an ASA in 56.3%.

Closure of the PFO

Twenty-eight procedures (68.3%) were performed under general anaesthesia; all were guided by TOE. Thirteen procedures (31.7%) were performed under local anaesthesia; of these, 12 were guided by TTE and one by intracardiac echocardiography (Fig. 6). All of the procedures were performed by venous femoral access. The success rate was 100%.

Different devices were used: the Amplatzer™ PFO occluder ($n = 24$); the Amplatzer™ cribriform occluder ($n = 6$); the Occlutech® Figulla® Flex II UNI occluder ($n = 6$); the Occlutech® Figulla® Flex II PFO occluder ($n = 3$); the Cardia® Intrasept™ PFO occluder ($n = 1$); and the Nit-Occlud® PFO occluder ($n = 1$) (Fig. 7). The device manufacturers and sizes are listed in Table 3.

Median fluoroscopy time was 4.14 (0.5–20) minutes: 4.38 minutes for the procedures under TTE, and 3.55 minutes for the procedures under TOE. Only three centres performed an injection with contrast agent, for five procedures, all with TTE guidance.

There was one periprocedural complication: a gas embolism responsible for a transient myocardial ischaemia with complete AVB. There were two instabilities of the device requiring replacement with a larger device: one procedure guided by TOE, and one guided by intracardiac echocardiography.

Postprocedural treatment

Thirty-three patients were treated with aspirin (80.5%) and five with an anticoagulant (12.2%): four with fluindione, and one with apixaban. The postprocedural treatment was not known for three patients. The five patients treated with anticoagulant had undergone PFO closure for stroke.

Immediate changes

Twenty-one patients (56.8%) had a complete occlusion on contrast TTE immediately after the procedure, of the 37 patients in whom it was investigated (Fig. 8). Two patients had transient migraines after the procedure. No cardiac complications were noted. Median duration of hospitalization was 2 (1–3) days.

Comparison of periprocedural TOE and TTE guidance

Compared with the patients who had a procedure guided by TTE, those who underwent TOE had a slightly lower body weight, while the duration of the fluoroscopy tended to be longer, although this was not significant. Both the device size/weight ratio and the percentage of residual shunting were also a little bit higher. These differences were not significant (Table 4).

The choice of TOE and TTE guidance was not linked to the number of procedures performed in the centre; rather, it was based only on the centre's practice. Among the four centres with the highest number of procedures, two performed their procedure exclusively under TOE, one performed half of the procedures under TTE and half under TOE and one performed a third under TTE and two thirds under TOE.

Changes at 1 year after the procedure

In our cohort, six patients had a PFO closure for < 1 year. Eleven patients (31.4%) retained significant residual shunting, diagnosed by TTE with contrast agent, of the 35 patients in whom it was investigated. Nineteen patients (76%) continued aspirin therapy (17 had undergone PFO closure for stroke, one for migraine and one for a left-to-right shunt), while six (24%) were no longer undergoing treatment (four had undergone PFO closure for stroke, one before the implantation of an endocavitary pacemaker and one for a left-to-right shunt); these data were not available for 16 patients. There were no complications, nor any cases of recurrent stroke at 1-year follow-up.

Changes at the last consultation at the interventional centre

Median duration of follow-up was 568 (37–5137) days. Two of 26 patients in whom it was investigated retained significant residual shunting, diagnosed by TTE with contrast agent. Eight patients (40%) continued treatment with aspirin (seven had undergone PFO closure for stroke, one for migraine) and 12 (60%) no longer received any treatment (nine had undergone PFO closure for stroke, one before the implantation of an endocavitary pacemaker and two for a left-to-right shunt); these data were not available for 21 patients. None of the patients exhibited complications or recurrent stroke during the follow-up.

Centre questionnaires

We next examined the practices at the different participating centres, to determine the way in which PFO is diagnosed and treated in France. In terms of diagnosis, two-thirds of the participating centres performed TTE with contrast agent (c-TTE) and one-third performed TOE. An ASA was systematically screened for during echocardiography.

The criteria for retaining the indication of closure differed between the centres: four centres required the presence of moderate-to-substantial shunting, irrespective of the anatomy of the PFO; for two centres the size of the PFO had to be > 3 mm and the shunt had to be substantial; whereas one centre required the existence of an ASA. For two centres, the anatomy of the PFO did not come into play for the indication.

In all centres, the cases were discussed by the cardiologist and the neurologist before undertaking PFO closure following a stroke or TIA. Four centres retained a systemic embolism other than in the brain as an indication for PFO closure, and two (25%) retained migraine as an indication.

Most centres (75%) performed their procedures under general anaesthesia, with systematic TOE guidance for 75% of the centres and TTE or TOE for 25%. Local anaesthesia was acceptable for an adolescent and cooperative patient in 62.5% of the centres; these procedures were usually guided by TTE, whereas one centre used intracardiac echocardiography.

The treatment, its duration and postoperative follow-up varied between the centres: all used aspirin; one centre combined aspirin with clopidogrel for a duration of 3 months; one centre continued with anticoagulant treatment if it was being used before the procedure. All centres saw the patients again for a consultation, with an electrocardiogram and TTE, 1 month and 1 year after device implantation.

Discussion

The foramen ovale is an interatrial shunt indispensable to foetal viability; it typically closes after birth by fusion of the septum primum to the septum secundum. This fusion occurs in a progressive manner over time, and can remain incomplete in one in every four adults, with an incidence that decreases with age: 34% at 30 years of age, 20% after 80 years of age [7].

The persistence of a PFO is associated with different pathological situations in adults, such as cryptogenic strokes, migraines, diving accidents and platypnoea-orthodeoxia syndrome [8-15]. The

need for PFO closure is hence now recognized in adults [1, 2] after affirmation of a cryptogenic stroke diagnosis by a neurologist, and confirmation of the indication by a joint assessment by the neurocardiology team [3, 16-18].

Cryptogenic strokes are rare in children, and associated risk factors are often present (e.g. thrombophilia) [19]. Involvement of the PFO has been shown in several case reports [2, 20, 21], and paradoxical embolism remains a diagnosis of exclusion [6, 19]. The RoPE Score [22], which is used to evaluate the risk of cryptogenic stroke in adults, cannot be used in the paediatric population, and the aetiological assessment needs to be exhaustive and multidisciplinary. Unlike the guidelines for adults, recommendations for the treatment of PFO after cryptogenic stroke in children are not currently available [1, 2].

There are no data regarding systemic embolisms in other areas (myocardial, kidney, limbs, etc.), but the approach in adults is typically the same as for a neurological injury [2, 9]. Similarly, the prevalence of PFO is more frequent in patients who experience migraine with aura [23]. In children, the prevalence is found to be much higher in cases of migraine with aura (50%) than in the general population (25%), while the difference is not significant in the absence of aura (35%) [24]. The relevance of PFO closure in this indication in adults has not been confirmed in several randomized studies [25, 26], although it is suggested by the observation of patients who underwent PFO closure for a stroke [27] and by a more recent meta-analysis (80% improvement) [28].

Experience in regard to PFO closure in children remains limited. The largest series reported to date included 153 patients, with a median age of 16 (5–19) years [29]. The procedure was indicated for migraines in 68% of cases, headaches without migraine in 16%, TIA in 28% and stroke in 16%. The devices used were an Amplatzer™ in 75% of cases and a Gore® septal occluder (Gore Medical, Flagstaff, AZ, USA) in 30%. After a median follow-up of 1 year, symptoms had improved in 93% of the patients, despite a rate of residual shunting of 19%. One endocarditis occurred 4 months after the implantation, requiring surgical removal of the prosthesis. Sel et al. also reported their experience in 17 patients with a median age of 11 years (10 after a TIA, four after a stroke and three for migraine), with clinical improvement in 15 patients [30].

Few poststroke series have been published, with small patient samples and limited follow-up. Ballerini et al. reported a series of 15 children who had undergone percutaneous PFO closure and received antiaggregation treatment with aspirin 2–3 mg/kg/day for 6 months, without complications or

recurrences [31]. Benedikt et al. reported a series of nine children (four after a stroke and five after a TIA), for whom the PFO was closed by an Amplatzer™ occluder, with success in eight cases out of nine (the unsuccessful case did not have a PFO, but an intrapulmonary shunt) [19]. Postimplantation treatment consisted of aspirin for 6 months, and there were no complications during follow-up of 6–21 months.

The occurrence of a cerebral abscess can also be explained by right-to-left shunt, which allows gut or dental microorganisms to pass into the cerebral circulation by short-circuiting the pulmonary circulation [32]. Approximately 20 case reports have been published in regard to adults – mostly elderly patients – and none involving children [32]; the authors favour closure of the PFO.

In our study, the indications for PFO closure were overall in keeping with the guidelines for adults: 76% poststroke after multidisciplinary assessment; and 4.8% after a cerebral abscess. Yet two centres also retained the indication of closure in cases of migraine with aura, and only one for a permanent left-to-right shunt. One centre retained an exceptional indication of preventative closure before placement of a pacemaker. There is also a report in the literature of PFO closure in twins with Hurler syndrome who had central lines: one after a stroke by a paradoxical embolism and the other for primary prevention [33]. Interestingly, there was no PFO closure indication for cyanosis in our study.

The diagnosis of PFO was made in a pragmatic manner in 72.2% by c-TTE. Indeed, in children, performing a TOE typically requires general anaesthesia, and the good echogenicity most often allows this invasive examination to be skipped for the diagnosis [10, 34].

More than two-thirds of the patients had general anaesthesia for the procedure, which could be guided by TOE. It should be noted that device size/weight ratio, fluoroscopy time and degree of residual shunting were lower in the TOE group, although the difference was not significant. Therefore, this approach could help with selection of the most accurate device, as oversizing has been reported to be associated with a risk of aortic erosion [35], and to minimize the risks linked to radiation [36]. The advantage of using TOE has also been reported for adults, with a reduction in fluoroscopy time and the rate of residual shunting at 6 months (8% vs 16.8%) [37]. It should be pointed out that only one centre used intracardiac imaging for PFO closure in children, whereas this method is used regularly and has been validated in adults [38]. The choice of TOE or TTE guidance was not linked to the number of procedures performed in the centre; rather, it was based only on the centre's practice.

Our study comprised two distinct periods: the first, until 2014, during which PFO closure in children was rare (on average, 0.8/year); and the second after 2015, with an average of 6/year. This is somewhat confusing, as studies showing the benefit of PFO closure after cryptogenic stroke were not published until the end of 2017 [3, 4]. Before this, the indications for adults were based on the 2007 guidelines from a group of cardioneurology experts [39].

The success rate of the procedure was 100%, and complications were rare, with a single periprocedural complication (a transient third-degree AVB secondary to a coronary gas embolism, which recovered spontaneously and without sequelae) and a requirement to change two unstable devices. There were no delayed complications – in particular, no aortic erosion, no endocarditis and no triggering of arrhythmia – whereas in the CLOSE study there was a 4.6% rate of supraventricular tachycardia [3] and in the meta-analyses the rate was 3.8–5.2% [40, 41]. As in adults, the treatment postprocedure and its duration are poorly codified, and vary from one centre to the next.

In adults, the rate of residual shunting, defined as the persistence of the passage of bubbles after closure of the PFO, varies from one series to the next, and decreases over time: 7% immediately postprocedure and 3% at 6 months in the series of Wintzer-Wehekind et al. [42], but 16% at 3 months and 11% at 9 months in the study by Moon et al. [43] and 7% at 6 months in the CLOSE study [3]. No correlation has been shown between the persistence of residual shunting and recurrent stroke. In our study, the rates of residual shunting of 43.2% immediately postprocedure and 31.4% at 1 year were much higher. These residual shunts were systematically screened for using c-TTE, and the detection of bubbles is probably better in children than in adults. The efficacy increased, however, over time, with a rate of permeability of just 7.7% at the last cardiac review. It should also be noted that our rate of recurrent stroke or TIA was 0%, with a median follow-up of 568 days or 1.55 years.

Study limitations

The limitations of our study are inherent to its retrospective nature, with a significant proportion of unavailable data, sometimes for more than half of the patients. Moreover, data were collected only from the French Congenital Catheterization Group of the FCPC, and also are not comprehensive. Similarly, we could not assess the proportion of patients aged < 18 years in each centre.

Conclusions

PFO closure is performed rarely in children because of the paucity of indications and the absence of guidelines for this population. In our study, the indication of PFO closure was mostly for pubescent patients (70.7%), poststroke (86.2%), for whom it appears to be appropriate to extrapolate the guidelines for adults. Despite the low number of subjects and its retrospective nature, our series confirms the useful role of c-TTE in diagnosing PFO. The procedure appears to be safe, as we noted a low rate of immediate and long-term complications. Moreover, following a neurological event, PFO closure in children and teenagers is effective, without recurrent stroke, despite a higher residual shunting rate compared with adult patients.

Sources of funding

The Electrophysiology and Heart Modelling Institute was supported by the French government (grant ANR-10-IAHU-04). The sponsor played no role in the study design, in the collection, analysis and interpretation of data, in the writing of the report or in the decision to submit the article for publication.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

- [1] Mas JL, Derex L, Guerin P, et al. Transcatheter closure of patent foramen ovale to prevent stroke recurrence in patients with otherwise unexplained ischaemic stroke: Expert consensus of the French Neurovascular Society and the French Society of Cardiology. *Arch Cardiovasc Dis* 2019;112:532-42.
- [2] Pristipino C, Sievert H, D'Ascenzo F, et al. European position paper on the management of patients with patent foramen ovale. General approach and left circulation thromboembolism. *Eur Heart J* 2019;40:3182-95.
- [3] Mas JL, Derumeaux G, Guillon B, et al. Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke. *N Engl J Med* 2017;377:1011-21.
- [4] Saver JL, Carroll JD, Thaler DE, et al. Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke. *N Engl J Med* 2017;377:1022-32.
- [5] Sondergaard L, Kasner SE, Rhodes JF, et al. Patent Foramen Ovale Closure or Antiplatelet Therapy for Cryptogenic Stroke. *N Engl J Med* 2017;377:1033-42.
- [6] Dowling MM, Ikemba CM. Intracardiac shunting and stroke in children: a systematic review. *J Child Neurol* 2011;26:72-82.
- [7] Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc* 1984;59:17-20.
- [8] Agarwal S, Bajaj NS, Kumbhani DJ, Tuzcu EM, Kapadia SR. Meta-analysis of transcatheter closure versus medical therapy for patent foramen ovale in prevention of recurrent neurological events after presumed paradoxical embolism. *JACC Cardiovasc Interv* 2012;5:777-89.
- [9] Giblett JP, Abdul-Samad O, Shapiro LM, Rana BS, Calvert PA. Patent Foramen Ovale Closure in 2019. *Interv Cardiol* 2019;14:34-41.
- [10] Khan R, Chan AK, Mondal TK, Paes BA, Thrombosis and Hemostasis in Newborns Group. Patent foramen ovale and stroke in childhood: A systematic review of the literature. *Eur J Paediatr Neurol* 2016;20:500-11.
- [11] Lamy C, Giannesini C, Zuber M, et al. Clinical and imaging findings in cryptogenic stroke patients with and without patent foramen ovale: the PFO-ASA Study. *Atrial Septal Aneurysm. Stroke* 2002;33:706-11.

- [12] Lechat P, Mas JL, Lascault G, et al. Prevalence of patent foramen ovale in patients with stroke. *N Engl J Med* 1988;318:1148-52.
- [13] Schneider B, Hofmann T, Justen MH, Meinertz T. Chiari's network: normal anatomic variant or risk factor for arterial embolic events? *J Am Coll Cardiol* 1995;26:203-10.
- [14] Schuchlenz HW, Weihs W, Horner S, Quehenberger F. The association between the diameter of a patent foramen ovale and the risk of embolic cerebrovascular events. *Am J Med* 2000;109:456-62.
- [15] Steiner MM, Di Tullio MR, Rundek T, et al. Patent foramen ovale size and embolic brain imaging findings among patients with ischemic stroke. *Stroke* 1998;29:944-8.
- [16] Carroll JD, Saver JL, Thaler DE, et al. Closure of patent foramen ovale versus medical therapy after cryptogenic stroke. *N Engl J Med* 2013;368:1092-100.
- [17] Mirzada N, Ladenvall P, Hansson PO, Eriksson P, Dellborg M. Recurrent stroke in patients with patent foramen ovale: An observational prospective study of percutaneous closure of PFO versus non-closure. *Int J Cardiol* 2015;195:293-9.
- [18] Riaz H, Khan MS, Schenone AL, Waheed AA, Khan AR, Krasuski RA. Transcatheter closure of patent foramen ovale following cryptogenic stroke: An updated meta-analysis of randomized controlled trials. *Am Heart J* 2018;199:44-50.
- [19] Benedik MP, Zaletel M, Meglic NP, Podnar T. Patent foramen ovale and unexplained ischemic cerebrovascular events in children. *Catheter Cardiovasc Interv* 2007;70:999-1007.
- [20] Filippi L, Palermo L, Pezzati M, et al. Paradoxical embolism in a preterm infant. *Dev Med Child Neurol* 2004;46:713-6.
- [21] Gunta S, Kamath S. A case of pulmonary embolism and stroke in a 16-year-old girl. *WMJ* 2012;111:58-60.
- [22] Kent DM, Ruthazer R, Weimar C, et al. An index to identify stroke-related vs incidental patent foramen ovale in cryptogenic stroke. *Neurology* 2013;81:619-25.
- [23] Lip PZ, Lip GY. Patent foramen ovale and migraine attacks: a systematic review. *Am J Med* 2014;127:411-20.
- [24] McCandless RT, Arrington CB, Nielsen DC, Bale JF, Jr., Minich LL. Patent foramen ovale in children with migraine headaches. *J Pediatr* 2011;159:243-7 e1.

- [25] Dowson A, Mullen MJ, Peatfield R, et al. Migraine Intervention With STARFlex Technology (MIST) trial: a prospective, multicenter, double-blind, sham-controlled trial to evaluate the effectiveness of patent foramen ovale closure with STARFlex septal repair implant to resolve refractory migraine headache. *Circulation* 2008;117:1397-404.
- [26] Tobis JM, Charles A, Silberstein SD, et al. Percutaneous Closure of Patent Foramen Ovale in Patients With Migraine: The PREMIUM Trial. *J Am Coll Cardiol* 2017;70:2766-74.
- [27] Wahl A, Praz F, Tai T, et al. Improvement of migraine headaches after percutaneous closure of patent foramen ovale for secondary prevention of paradoxical embolism. *Heart* 2010;96:967-73.
- [28] Shi YJ, Lv J, Han XT, Luo GG. Migraine and percutaneous patent foramen ovale closure: a systematic review and meta-analysis. *BMC Cardiovasc Disord* 2017;17:203.
- [29] Menon SC, Grove A, McFadden M, Korgenski KE, Cowley CG. Clinical practice, resource utilization, and outcomes of device closure of patent foramen ovale in pediatrics. *Pediatr Neurol* 2014;50:213-7.
- [30] Sel K, Aykan HH, Duman D, et al. Transcatheter closure of the patent foramen ovale in children: intermediate-term follow-up results. *Cardiol Young* 2017;27:1545-9.
- [31] Ballerini L, Cifarelli A, Ammirati A, Gimigliano F. Patent foramen ovale and cryptogenic stroke. A critical review. *J Cardiovasc Med (Hagerstown)* 2007;8:34-8.
- [32] Horiuchi Y, Kato Y, Dembo T, Takeda H, Fukuoka T, Tanahashi N. Patent foramen ovale as a risk factor for cryptogenic brain abscess: case report and review of the literature. *Intern Med* 2012;51:1111-4.
- [33] Hill J, Preminger T. Percutaneous PFO closure for paradoxical stroke in 8-kg twins. *Catheter Cardiovasc Interv* 2014;84:110-3.
- [34] Hubail Z, Lemler M, Ramaciotti C, Moore J, Ikemba C. Diagnosing a patent foramen ovale in children: is transesophageal echocardiography necessary? *Stroke* 2011;42:98-101.
- [35] Amin Z, Hijazi ZM, Bass JL, Cheatham JP, Hellenbrand W, Kleinman CS. PFO closure complications from the AGA registry. *Catheter Cardiovasc Interv* 2008;72:74-9.
- [36] Miglioretti DL, Johnson E, Williams A, et al. The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk. *JAMA Pediatr* 2013;167:700-7.

- [37] Scacciatella P, Meynet I, Giorgi M, et al. Angiography vs transesophageal echocardiography-guided patent foramen ovale closure: A propensity score matched analysis of a two-center registry. *Echocardiography* 2018;35:834-40.
- [38] Kavvouras C, Vavuranakis M, Vaina S, et al. Intracardiac echocardiography for percutaneous patent foramen ovale and atrial septal defect occlusion. *Herz* 2019;44:445-9.
- [39] Albucher JF, Chaine P, Mas JL, et al. [Consensus about indications of endovascular closure of the patent foramen ovale after an ischemic brain stroke]. *Arch Mal Coeur Vaiss* 2007;100:771-4.
- [40] Johnson JN, Marquardt ML, Ackerman MJ, et al. Electrocardiographic changes and arrhythmias following percutaneous atrial septal defect and patent foramen ovale device closure. *Catheter Cardiovasc Interv* 2011;78:254-61.
- [41] Udell JA, Opatowsky AR, Khairy P, et al. Patent foramen ovale closure vs medical therapy for stroke prevention: meta-analysis of randomized trials and review of heterogeneity in meta-analyses. *Can J Cardiol* 2014;30:1216-24.
- [42] Wintzer-Wehekind J, Alperi A, Houde C, et al. Long-Term Follow-Up After Closure of Patent Foramen Ovale in Patients With Cryptogenic Embolism. *J Am Coll Cardiol* 2019;73:278-87.
- [43] Moon J, Kim M, Oh PC, et al. Residual Shunt after Patent Foramen Ovale Device Closure in Patients With Cryptogenic Stroke: Serial Bubble Contrast Transesophageal Echocardiography Data. *J Stroke Cerebrovasc Dis* 2019;28:347-53.

Figure legends

Figure 1. Number of patent foramen ovale closures in children per participating centre.

Figure 2. Number of patent foramen ovale closures in children per year.

Figure 3. Indications for patent foramen ovale (PFO) closure in children. L-R: left-to-right.

Figure 4. Diagnosis of patent foramen ovale by transthoracic echocardiography with contrast injection; apical view. A. At rest; moderate right-to-left shunting. B. After Valsalva manoeuvre; massive right-to-left shunting.

Figure 5. Anatomy of the patent foramen ovale (PFO) by transoesophageal echocardiography; midesophageal view. A. Short-axis aortic view (70 °): PFO, with eustachian valve (arrow). B. Bicaval-tricuspid valve view (90 °): left-to-right colour shunt (arrow). C. Bicaval-tricuspid valve view (100 °): tunnel. D. Short-axis aortic view (70 °): size of PFO.

Figure 6. A–D. Procedural guidance by intracardiac echocardiography A. Patent foramen ovale (PFO). B. PFO with guidance. C. PFO closed by device. D. Fluoroscopy during device release. E–H. procedural guidance by transoesophageal echocardiography; short-axis aortic view (70 °). E. PFO. F. PFO with guidance. G. PFO closed by device. H. Fluoroscopy after device release.

Figure 7. Three of the devices used. A. Amplatzer™ PFO occluder (courtesy of Abbott; © 2019 Abbott; all rights reserved). B. Figulla® Flex II PFO occluder (Occlutech® Figulla® septal occluder [OFSO]; Occlutech GmbH Jena, Germany). C. Nit-Occlud® PFO occluder (PFM Medical AG, Cologne, Germany).

Figure 8. Postprocedure transthoracic echocardiography (TTE); apical view. A. Correct positioning of the device. B. TTE with contrast agent; no residual shunt.

Table 1 Indication for patent foramen ovale closure in pubescent and prepubescent subgroups.

Indication	Subgroup	Number (%)
TIA/stroke	Pubescent patients	25 (81)
	Prepubescent patients	6 (19)
Left-to-right shunt	Pubescent patients	3 (50)
	Prepubescent patients	3 (50)
Migraine	Pubescent patients	1
	Prepubescent patients	0
Cerebral abscess	Pubescent patients	0
	Prepubescent patients	2
Preimplantation endocavitary pacemaker	Pubescent patients	0
	Prepubescent patients	1

TIA: transient ischaemic attack.

Table 2 Anatomy of the patent foramen ovales.

		Number (%)
Shunt size (<i>n</i> = 14, 34.1%)	Moderate	8 (57)
	Substantial	6 (43)
PFO size (mm) (<i>n</i> = 13, 31.7%)	< 3	4 (31)
	3–5	6 (46)
	> 5	3 (23)
ASA (<i>n</i> = 32, 78.1%)	Yes	18 (56)
	No	14 (44)
Tunnel (<i>n</i> = 15, 36.6%)	Yes	7 (47)
	No	8 (53)

ASA: atrial septal aneurysm; PFO: patent foramen ovale.

Table 3 Device sizes and number used.

Device (manufacturer)	Specific device used	Device size (mm)	Number
Amplatzer™ (AGA Medical Corp., Plymouth, MN, USA)	Amplatzer™ PFO occluder (<i>n</i> = 24, 59%)	35	6
		25	17
		18	1
	Amplatzer™ cribriform occluder (<i>n</i> = 6, 15%)	35	2
		25	3
		18	1
Occlutech® (OFSO; Occlutech GmbH, Jena, Germany)	Occlutech® Figulla® Flex II UNI occluder (<i>n</i> = 6, 15%)	28.5	4
		33	2
	Occlutech® Figulla® Flex II PFO occluder (<i>n</i> = 3, 7%)	23/25	2
		27/30	1
Cardia® (Cardia Inc., Burnsville, MN, USA)	Cardia® Intrasept™ PFO occluder (<i>n</i> = 1, 2%)	20	1
Nit-Occlud® (PFM Medical AG, Cologne, Germany)	Nit-Occlud® PFO occluder (<i>n</i> = 1, 2%)	30	1

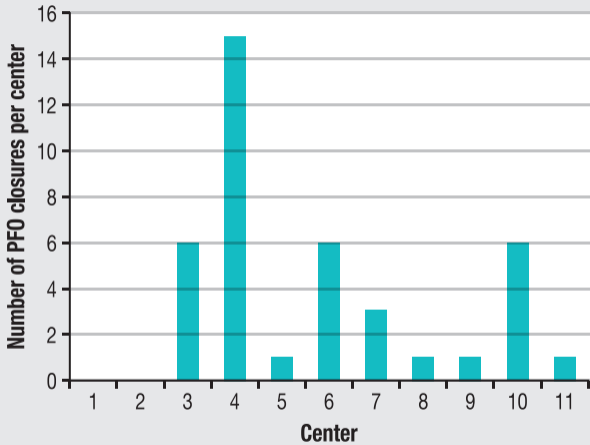
OFSO: Occlutech® Figulla® septal occluder; PFO: patent foramen ovale.

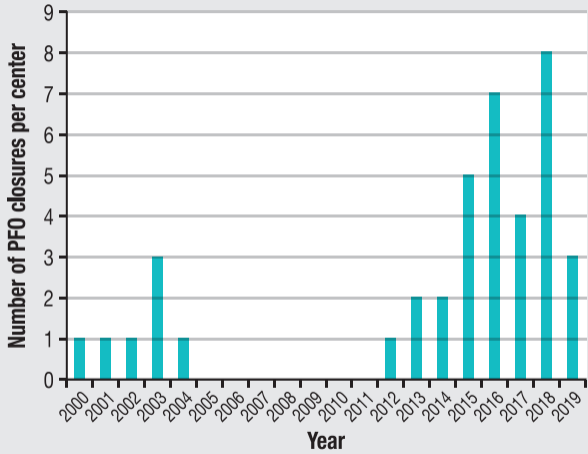
Table 4 Comparison of periprocedural transoesophageal and transthoracic echocardiography guidance.

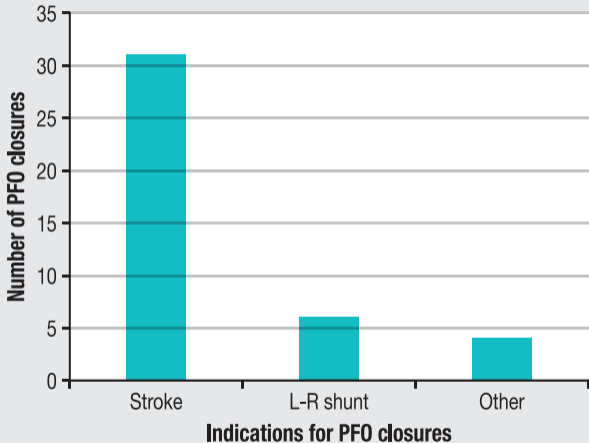
	TOE	TTE	<i>P</i>
Weight (kg)	52 (17–71)	51 (19–67)	0.65
Fluoroscopy time (minutes)	3.55 (0.5–11)	4.38 (1.55–20)	0.74
Device/weight ratio (mm/kg)	0.5 (0.32–1.94)	0.66 (0.37–1.3)	0.83
Residual shunting (%)	40	54.5	0.34

Data are expressed as median (minimum–maximum) or %. TOE: transoesophageal echocardiography;

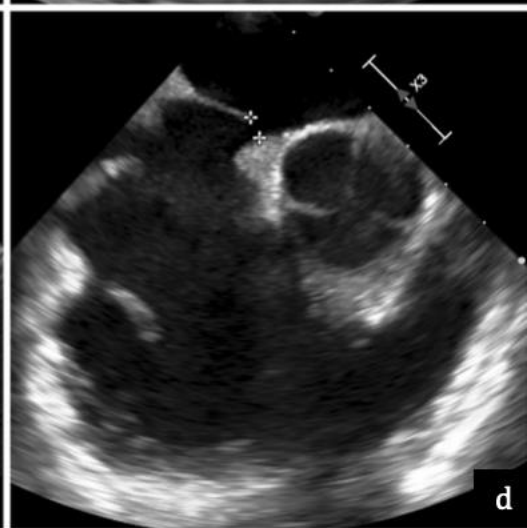
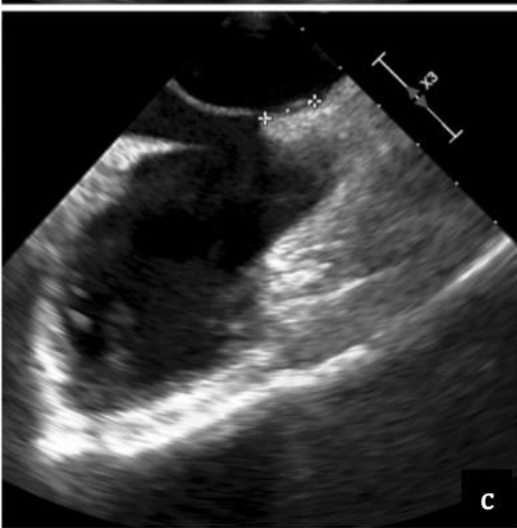
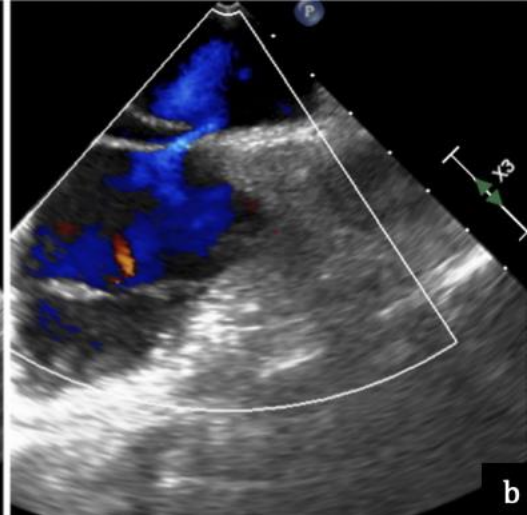
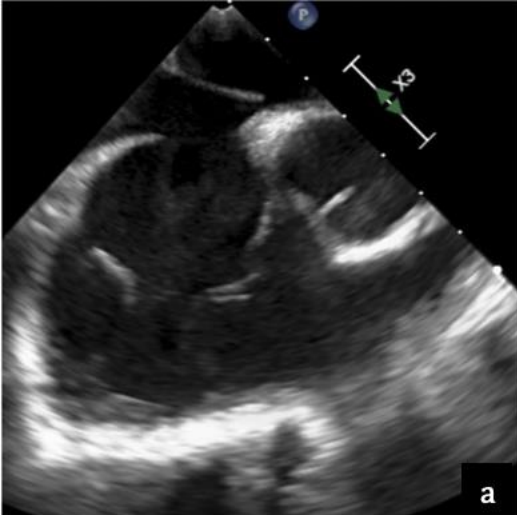
TTE: transthoracic echocardiography.





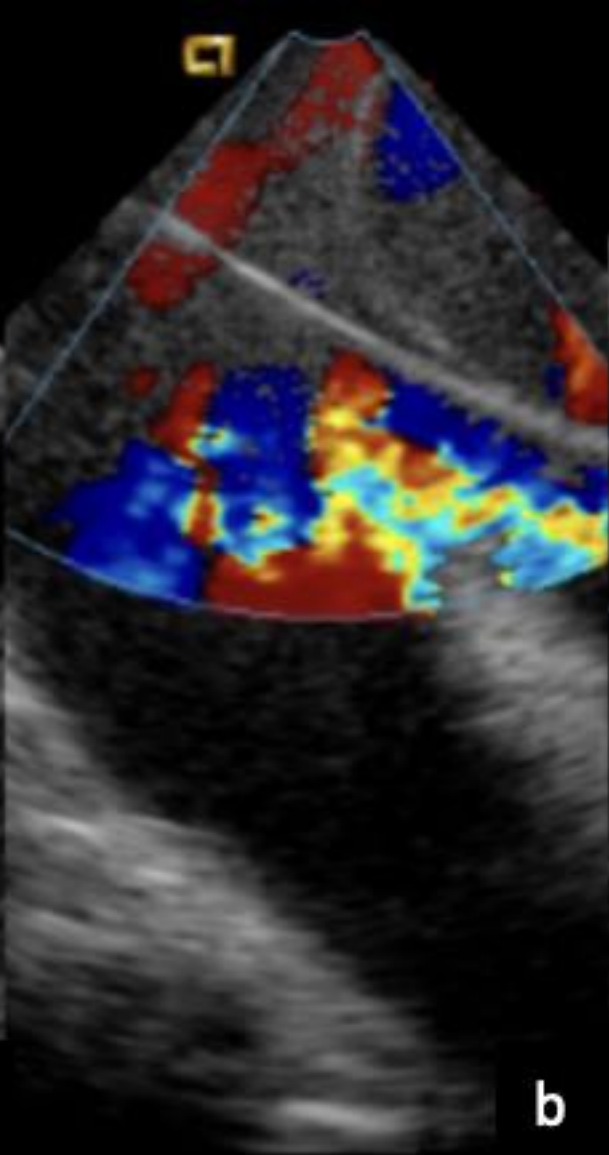




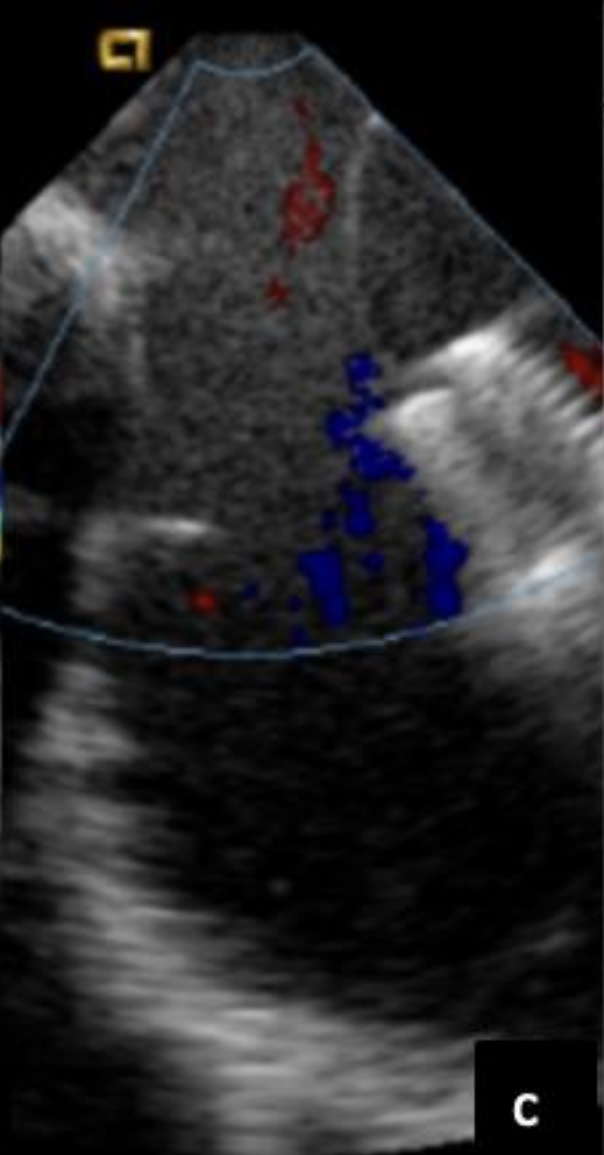




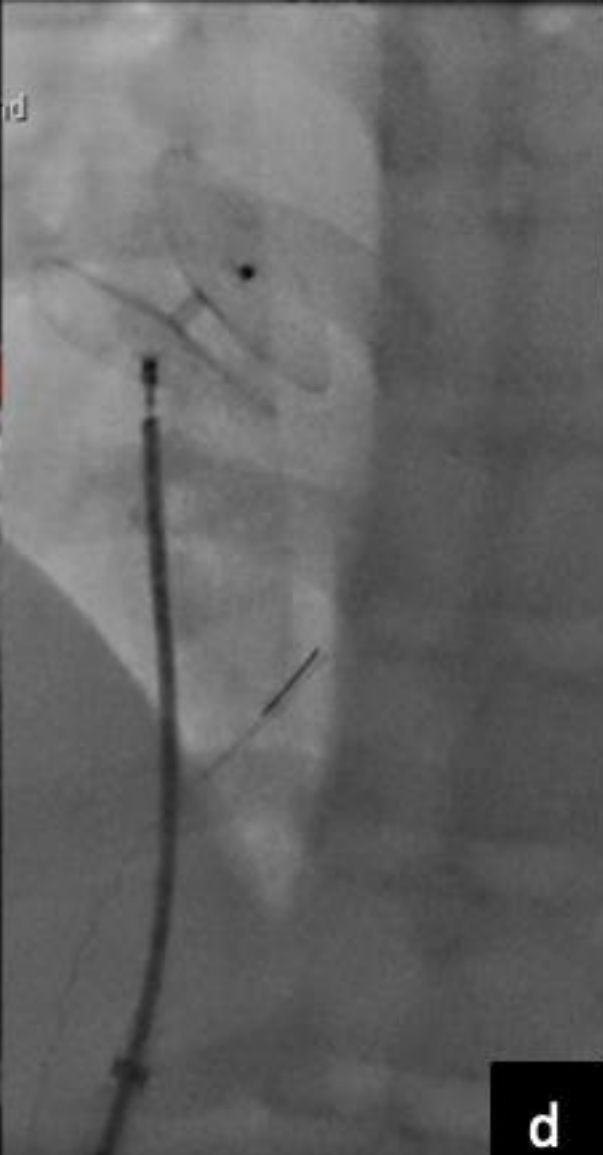
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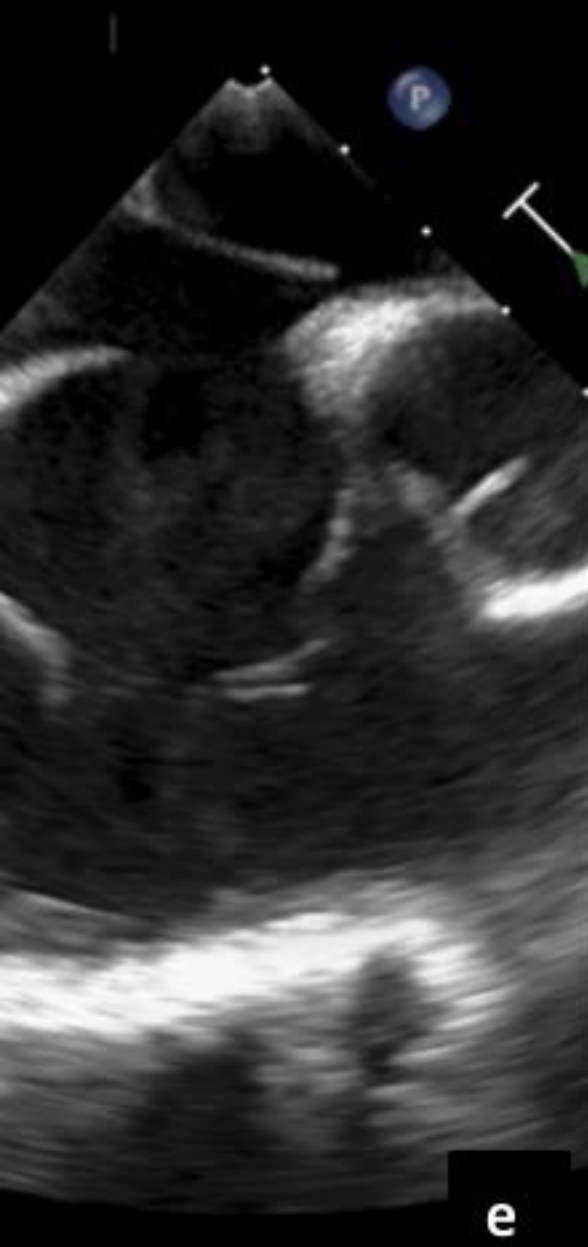
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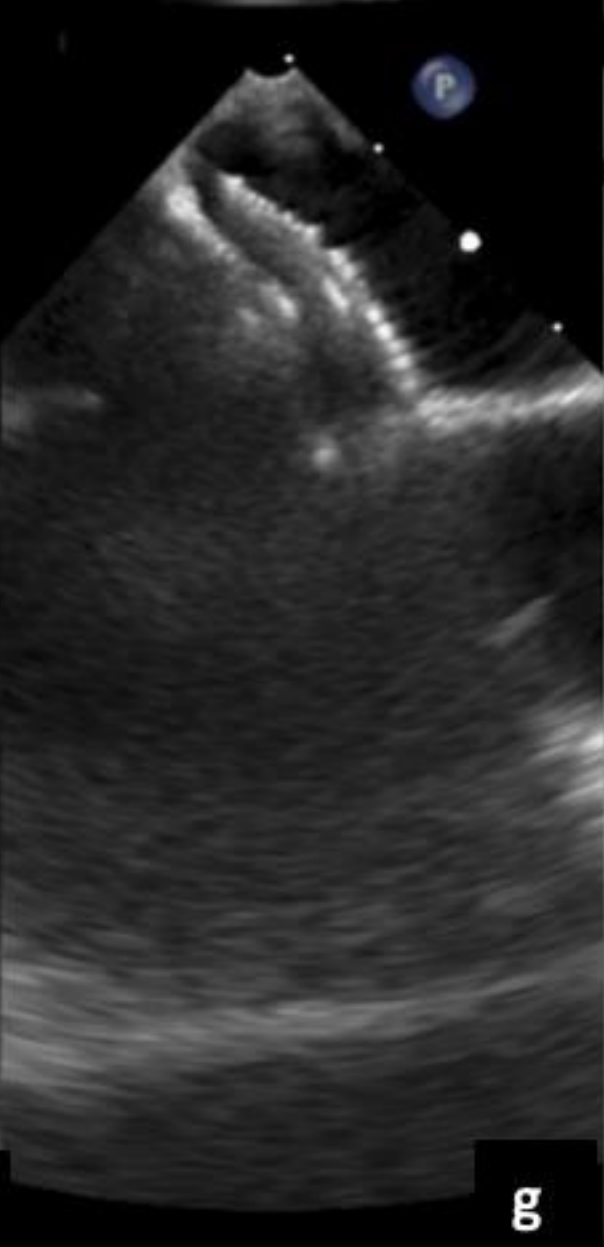
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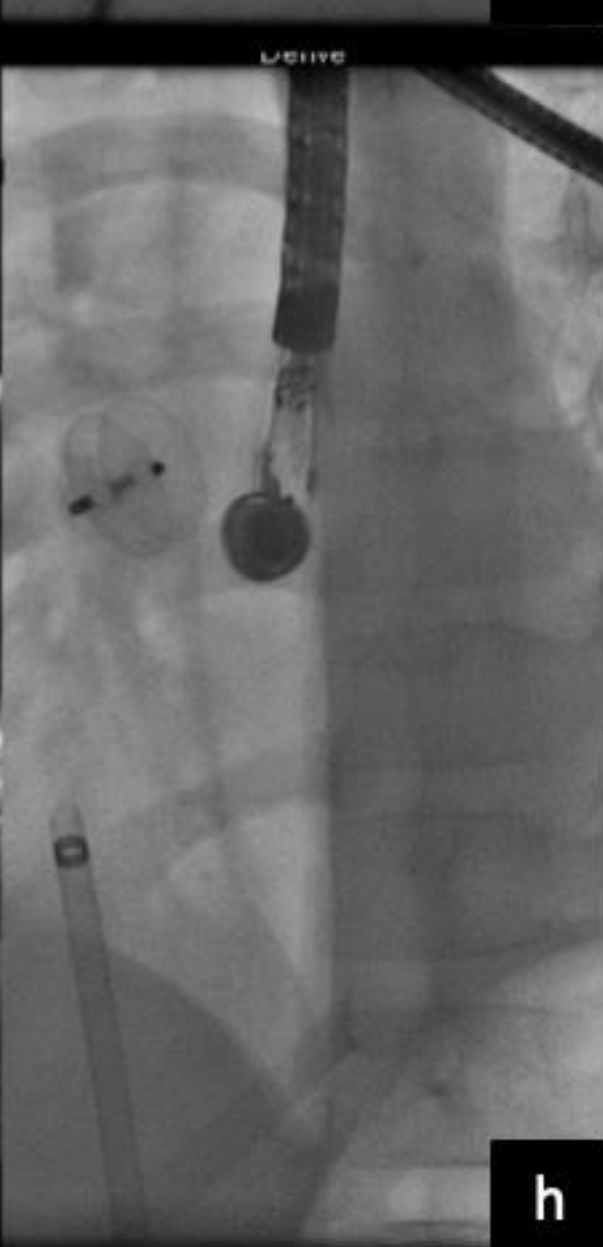
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