KARDIOLOGIA POLSKA

Polish Heart Journal
The Official Peer-reviewed Journal of the Polish Cardiac Society since 1957

Online first
This is a provisional PDF only. Copyedited and fully formatted version will be made available soon

ISSN 0022–9032 e-ISSN 1897–4279

Headache after transcatheter closure of atrial septal defect: An attempt to explain its origin in pediatric population

Authors: Sebastian Smerdziński, Michał Gałeczka, Filip Tyc, Mateusz Knop, Jacek Białkowski, Roland Fiszer

Article type: Original article

Received: April 4, 2022

Accepted: December 9, 2022

Early publication date: December 27, 2022

Headache after transcatheter closure of atrial septal defect: An attempt to explain its origin in pediatric population

Short title: Headache after transcatheter ASD closure in children

Sebastian Smerdziński[1, 2], Michał Gałeczka[1], Filip Tyc[1, 2], Mateusz Knop[1, 2], Jacek Białkowski[1, 2], Roland Fiszer[1, 2]

[1]Department of Congenital Heart Defects and Pediatric Cardiology, Silesian Center for Heart Diseases, Zabrze, Poland
[2]Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland

Correspondence to:
Sebastian Smerdziński, MD,
Department of Congenital Heart Defects and Pediatric Cardiology,
Silesian Center for Heart Diseases,
M Skłodowskiej-Curie 9, 41–800 Zabrze, Poland,
phone: +48 37 33 669,
e-mail: smerdzinski@gmail.com

WHAT'S NEW?

Headaches following transcatheter closure of atrial septal defect (ASD) are a known complication. Their etiology has not been fully elucidated. In many studies, the authors emphasized the role of nickel released into the serum from the implant. In our work, we have also proved the impact of balloon calibration of ASD diameter on the occurrence of postoperative headaches in these patients. To our best knowledge, this is the first paper to report influence of balloon calibration on headache episodes after ASD closure. Operator experience with the calibration balloon can minimize the frequency of headaches. The procedure itself should be reserved for special cases, and the ASD dimensioning should be assessed by other techniques, especially three-dimension echocardiography.

ABSTRACT

Background: Transcatheter closure of atrial septal defect (ASD) has become the treatment of choice for most patients. About 5% of them after the procedure suffer from the transient headache episodes (THE), the etiology of which is unclear.

Aims: To evaluate risk factors for THE occurrence after transcatheter closure of ASD in the pediatric population.

Methods: 840 patients, after transcatheter ASD closure, with nitinol devices, from a single center, were included in retrospective analysis. THE was defined as occurring up to 24 hours after procedure. A logistic regression model including age, weight, ASD diameter, device size, presence of nitinol coating on device, fluoroscopy time, application of balloon calibration, device oversizing and residual shunt after 24 hours was created to evaluate risk factors for THE occurrence.

Results: There were 40 patients (females 70%) with THE (4.8%). Median age was 13 (7.35–16) years. 40 patients (4.8%) with THE. Female 70%, male 30%. Median age 13 (7.35–16) years. Among patients with headache BC was performed more frequently (82.5% vs. 43.3%; *P* <0.001), the balloon waist median (interquartile range [IQR]), 19 (16–22) mm vs. 15 mm (12–18) mm; *P* <0.001 and device size median (IQR), 18 (13.5–22) mm vs. 14 (11–17) mm; *P* <0.001 were larger and the residual shunt after 24 hours (12.5% vs. 4.9%; *P* = 0.03) and a year (7.5 vs. 1.0%; *P* <0.001) was more frequent. ASD size and prevalence of double/multiple ASD were similar in both groups. Age, application of BC, no nickel release protection, duration of fluoroscopy and device oversizing were predictors of THE (*P* <0.001).

Conclusions: Balloon calibration during percutaneous ASD closure and absent nickel release protection layer on the device are risk factors of headache occurrence in the early postprocedural period.

Key words: balloon calibration, headache

INTRODUCTION

Atrial septal defect (ASD) is one of the most common congenital heart diseases (CHD) and accounts for 10%–15% of all CHD. Transcatheter closure of ASD has become the treatment of choice in most patients [1, 2] however, defects too large for device closure or with an unfavorable anatomy still need surgical approach. However, there are defects still requiring a surgical approach, e.g., too large for device closure or the ones with an unfavorable anatomy.

Recommended treatment age of ASD is 3–6 years old [3]. Typical symptoms like fatigue, loss of exercises tolerances and supraventricular arrythmias build up slowly and aren't present till adulthood [4]. Small defects (below 8mm diameter) may spontaneously close. Nevertheless, in some infants we observe growth retardation [5] and larger ASDs may increase in size as the child grows which force us to perform percutaneous closure in selected younger patients [3].

Most of the devices designed for ASD closure are constructed with a nitinol (titanium and nickel alloy) self-expandable and double-disc wire mesh, filled with a polypropylene fabric, which seals the implant [6]. The general principle when selecting the device size is that it should match or slightly exceed the ASD diameter [7]. Ultrasonography, especially three-dimensional, is the preferred method to evaluate the ASD size, morphology, and rims. Transesophageal echocardiography (TEE) is the most widely used to navigate during ASD device closure, however, transthoracic or intracardiac ultrasonography is also feasible [8]. In selected defects evaluation by ultrasonography alone is insufficient (particularly in small children, in whom three-dimensional imaging is impossible), which makes a balloon calibration (BC) of the ASD a proper approach [9, 10]. The most severe complications of ASD device closure, namely, device embolization and erosion, may result from under- and overestimation of device size (mismatch) which is a well-known hazard [11]. Up to 5% of patients after transcatheter ASD closure suffer from transient headache episodes (THE) [12, 13]. Etiology of this phenomenon has not been clearly explained so far, however, few hypotheses have arisen (described in the discussion section). The aim of the study was to evaluate risk factors for THE occurrence after transcatheter closure of ASD in the pediatric population.

METHODS

Study design

Among over 1500 consecutive patients who underwent transcatheter closure of ASD between 1997 and 2017 in a single tertiary center [14], all 851 pediatric patients (up to 18 years old) were included in the retrospective, descriptive and nonrandomized analysis. Medical records, hemodynamic and echocardiographic data, periprocedural and one-year follow-up results were obtained from our registry to predefine the risk factors for THE occurrence in periprocedural period. Unsuccessful device implantation, device embolization (regardless of the method of retrieval and subsequent defect closure), major periprocedural complications (noted within 24 hours) and nickel skin allergy were the exclusion criteria. Death, stroke, tamponade, and severe arrhythmias were qualified as major complications. The indications and contraindications for ASD closure were consistent with the American Heart Association statement [15]. The study was approved by the university research ethics committee. Written informed consent was obtained from all caregivers (and children >16 years old) prior to the procedure.

Data analysis

Statistical analyses were performed using Statistica 13.3 software (StatSoft Inc.). All continuous variables are expressed as median with IQR (interquartile range [IQR]), and categorical data are presented as frequencies and percentages. The data distribution was tested using a Shapiro–Wilk test. The cohort was divided in two groups in terms of THE occurrence. Data were compared using the Student t-test, $\chi 2$, Mann–Whitney tests, as appropriate. A stepwise backward_logistic regression model was created to evaluate the variables affecting the occurrence of THE with MedCalc software (MedCalc Software Ltd, Ostend, Belgium). Variables included in the model were: age, weight, ASD diameter, device size, presence of device coating to protect from nickel release, duration of fluoroscopy, application of balloon calibration, degree of device oversizing (device size to ASD diameter ratio) and presence of residual shunt after 24 hours. The regression model was statistically significant with P <0.001, AUC of 0.847; 95% confidence interval (CI), 0.821–0.871. A P-value <0.05 was considered to indicate a statistically significant result.

RESULTS

Total number of 840 patients were included in further analysis. There were 571 female (68.0%) and 269 male (32.0%) patients. The median (IQR) age was 5.5 (3–11) years and median (IQR) weight was 20 (14.5–28) kilograms. Overall, 11 patients were excluded. Four patients (0.5%) were

excluded due to implantation failure: in three small children the device was withdrawn due to improper position (large defects with insufficient rims) and in one teenager with large defect the 34 mm device caused significant mitral regurgitation and 2nd degree atrioventricular block — after removal the abnormalities resolved. Six patients were excluded due to device embolization (two patients needed urgent surgery), one patient was excluded due to periprocedural tamponade. A group of five patients (0.6%) after previous surgical closure of ASD were qualified for transcatheter closure due to significant residual shunt; a group of seven patients (0.8%) with right ventricle dysfunction and bidirectional shunt through the defect were qualified for transcatheter closure due to cyanosis. In one patient ASD was closed in a transplanted heart, another patient had dextrocardia. Overall, 671 patients (79.9%) had single, and 169 patients (20.1%) had double/multiple ASD. In case of 63 patients (7.5%) the atrial septum was qualified as aneurysmatic. In case of 33 patients (3.9%) concomitant heart defects were confirmed and the most common were: pulmonary valve stenosis (PS) in 19 patients, patent ductus arteriosus (PDA) in 4 patients and ventricular septal defect (VSD) in 4 patients.

All procedures were performed in the standard manner described elsewhere [7], under general anesthesia and TEE guidance, via femoral approach, after heparin (100 IU/kg bolus) and antibiotic administration. After success ASD closure heparinization (controlled by activated partial thromboplastin time [APTT]) was continued for 48 hours and antiplatelet therapy (acetylsalicylic acid 3–5 mg/kg/daily) for 6 months was applied. Median (IQR) ASD diameter assessed on TEE was 10 (8–13) mm. BC was performed in 379 (45.1%) selected cases. Predominantly the Amplatzer sizing balloon was used and in almost all patients the ‘stop flow’ technique was applied. BC was used in case of aneurysmatic septum, double/multiple morphology and in large defects. The median (IQR) balloon waist diameter (assessed on both TEE and fluoroscopy) was 15 (12–18) mm. Different nitinol wire mesh occluders were used depending on the procedure year, availability and operator’s preference: Amplatzer septal occluder (ASO) in 685 (81.5%) (including 9 patients with Amplatzer Cribriformis occluder), Hyperion in 52 (6.2%), Cocoon in 29 (3.5%) Cardi-o-Fix in 25 (3.0%), Figulla in 21 (2.5%), HeartR in 17 (2.0%) and Cera in 11 (1.3%) patients were applied. ASO applied before 2014 and HeartR devices did not have protection against nickel release (n = 570, 67.9%). Median (IQR) device diameter was 14 (11–17) mm. In 8 patients pulmonary balloon valvuloplasty and in one patient PDA closure with a coil were performed simultaneously at the same catheterization, and those patients were not excluded from analysis.

Median (IQR) fluoroscopy time was 3.1 (2.2–5) minutes. THE associated with the procedure were defined as occurring up to 24 hours after ASD closure, of more than mild intensity, not reported in anamnesis and lasting no more than 24–48 hours. Control transthoracic echocardiography was performed routinely after 24 hours, before discharge, after 7 days, after one, six, and twelve months. Residual shunts assessed after 24 hours and after a year were analyzed (observed in, respectively, 5.2% and 1.3% patients, and trivial/insignificant in all of them).

There was a total of 40 patients (females 68%) with THE (4.8%) in the population of 840 pediatric patients after percutaneous ASD closure. Patients with THE vs. without THE were older median (IQR) 13 (7.35–16) years old vs. 5 (3–10) years old (P <0.001) and with higher weight median 45 (22.4–54.5) kg vs. 19 (14–37) kg (P <0.001); there were no difference regarding the sex. Size of the ASD measured in TEE was similar in patients with and without THE median 12 (8–14.5) mm vs. 10 (8–13) mm (P = 0.19). The prevalence of double/multiple ASD was similar in both groups (29.0% in patients with THE vs. 25.1% without THE; P = 0.71). Among patients with THE the balloon calibration was performed more frequently (82.5 vs. 43.3%; P < 0.001) and the balloon waist was larger median 19 (IQR 16-22) vs. 15 (IQR 12-18) mm; P <0.001). The difference between the balloon waist and the ASD diameter measured in TEE was higher in THE group median (IQR) 6 (5–7) mm vs. 4 (3–6) mm (P <0.001). Also, the device diameter was larger in THE group median (IQR) 18 (13.5–22) mm vs. 14 (11–17) mm (P <0.001). The prevalence of residual shunt after 24 hours (12.5% vs. 4.9%; P = 0.03) and a year (7.5 vs. 1.0%; P <0.001) was higher in the group with THE. Above data were presented in Table 1. A stepwise backward logistic model revealed that age, application of calibration balloon, no nickel release protection, duration of fluoroscopy and device oversizing were predictors of THE (Figure 2). Results of the logistic regression model are presented in Table 2. Except short supraventricular tachycardia and transient AV II block (did not required pharmacotherapy or pacing) any others postprocedural complications in THE patients haven't been noted.

DISCUSSION

To our best knowledge, this is the first paper to report influence of balloon calibration on headache episodes after ASD closure. So far one of the most popular hypotheses of THE occurrence after ASD transcatheter closure is a transient increase of serum level of nickel after the device deployment [3, 12, 16]. Nickel together with titanium are components of the alloy from which

most devices are made. To minimize nickel release to serum, the following occluders have different protective layers: Intaglio layer in Amplatzer (after 2014), pre-oxidized nitinol in Hyperion, titanium nitride in Cera and platinum in Cocoon. All of the HeartR occluders as well as Amplatzer devices manufactured before 2014 were produced without any protective layer on the nitinol wire. Typically, skin is the target organ for nickel, which provokes allergic eczema or dermatitis. None of our pediatric patients had an allergic history related to nickel before ASD closure. In our study, absent protective layer before nickel release was found to be a factor contributing to the occurrence of THE. THE was reported in only two patients in whom a device with nickel release protection was applied (Figulla and Cardi-o-Fix). In the remaining 38 THE patients the Amplatzer device (without Intaglio layer) was implanted. There was no THE after 2014 in the analyzed cohort. The highest nickel serum level persists only for a few weeks and then normalizes due to formation of oxide film and calcium phosphate layer [16] which could explain the fleeting character of THE.

Limitations of our retrospective study was no possibility to measure level of nickel and other biochemical parameters in THE patients. We were able to explain this phenomenon only by statistical analysis.

Researchers from Clinico San Carlos associate THE with microembolism. In their opinion headaches might result from a thrombotic substrate forming on the left-sided disk [13]. Perhaps this mechanism explains the role of BC in headache inducement as the balloon surface (even under proper heparinization confirmed with APTT) is a suitable surface for thrombi formation (Figure 1). Longer procedure time (indirectly expressed as fluoroscopy time) was also associated with risk for THE. For this reason, in our Center, we try to withdraw the balloon from the left atrium as soon as possible after defect calibration. Interestingly and regarding microembolism, logistic regression did not find residual leak after 24 hours to be a risk factor for THE, although in THE patients residual shunt in the first 24 hours and in one-year follow-up occurred more often.

Also, Wallace et al. approved microembolic thesis using transcranial doppler technique. They observed much more signals during inflation of the balloon, vascular sheath placement and device upload than in other procedure phases like hemodynamic measurements [17].

Another interesting, potential cause of THE is elevated serum level of natriuretic peptide because of atrial wall deformation after device implantation [12, 13]. Possibly, a similar wall deformation can be produced by an inflated balloon.

Carlson and co-authors noted that overestimation of the implant size increases the complication rate, but in their study, headaches were not mentioned literally [18].

It seems that BC has a significant impact on the occurrence of THE. It is worth mentioning that balloon overinflation, and thus overestimating the implant size, may result in erosion especially in small children with low body weight [3].

On the other hand, small implants increase embolization hazard and more frequently give residual leak after implantation [18]. Certainly, in selected cases, the BC will still be helpful. In our opinion the procedure requires balloon removal as soon as possible. Moreover, precise balloon inflation ('stop flow' technique) may minimize the problems described in the article. All observed conclusions were implemented in our institution.

Influence of BC on THE occurrence has not been investigated so far [12]. No cases of persistent neurological deficits have been reported in literature. As well in our follow-up lasting mean 29 months (range 6–84). Except standard antiplatelet therapy (acetylsalicylic acid 3–5 mg/kg daily) any other treatment hasn't been necessary. Some centers recommend double antiplatelet therapy on these patients [17, 19].

There is a possibility of underestimating THE in pediatric patients, especially in the youngest children who cannot clearly describe their symptoms. Three-dimension TEE to select the device size is an interesting alternative to BC as it is less invasive [20]. The operator's experience of BC technique may minimize risk of THE or even eliminate necessity of BC using.

Article information

Conflict of interest: None declared.

Funding: None.

REFERENCES

1. King TD, Thompson SL, Steiner C, et al. Secundum atrial septal defect. Nonoperative closure during cardiac catheterization. JAMA. 1976; 235(23): 2506–2509, indexed in Pubmed: 946659.
2. Guidelines for the Management of Congenital Heart Diseases in Childhood and Adolescence. Cardiol Young. 2017; 27(S3): S1–S105, doi: 10.1017/S1047951116001955, indexed in Pubmed: 28972464.
3. Grygier M, Sabiniewicz R, Smolka G, et al. Percutaneous closure of atrial septal defect: a consensus document of the joint group of experts from the Association of Cardiovascular Interventions and the Grown-Up Congenital Heart Disease Section of the Polish Cardiac Society. Kardiol Pol. 2020; 78(10): 1066–1083, doi: 10.33963/KP.15629, indexed in Pubmed: 33016689.
4. Kubicka K, Kawalec W. Pediatric Cardiology [in Polish]. Warszawa 2003.
5. Knop MT, Białkowski J, Szkutnik M, et al. Transcatheter closure of atrial septal defects type 2 in children under three years of age. Kardiol Pol. 2018; 76(8): 1257–1262, doi: 10.5603/KP.a2018.0113, indexed in Pubmed: 29862489.
6. Walsh KP, Maadi IM. The Amplatzer septal occluder. Cardiol Young. 2000; 10(5): 493–501, doi: 10.1017/s1047951100008180, indexed in Pubmed: 11049125.
7. Masura J, Gavora P, Formanek A, et al. Transcatheter closure of secundum atrial septal defects using the new self-centering amplatzer septal occluder: initial human experience. Cathet Cardiovasc Diagn. 1997; 42(4): 388–393, doi: 10.1002/(sici)1097-0304(199712)42:4<388::aid-ccd7>3.0.co;2-7, indexed in Pubmed: 9408617.
8. The Amplatzer septal occluder and delivery system instruction for use. Available online: www.accessdata.fda.gov/cdrh_docs/pdf/P000039c.pdf. [Access: December 27, 2022].
9. Bergersen L, Foerster S, Marshall AC, et al. Congenital heart disease. Springer 2009.
10. Du ZD, Cao QL, Rhodes J, et al. Choice of device size and results of transcatheter closure of atrial septal defect using the amplatzer septal occluder. J Interv Cardiol. 2002; 15(4): 287–292, doi: 10.1111/j.1540-8183.2002.tb01105.x, indexed in Pubmed: 12238424.
11. Amin Z, Hijazi ZM, Bass JL, et al. Erosion of Amplatzer septal occluder device after closure of secundum atrial septal defects: review of registry of complications and recommendations to minimize future risk. Catheter Cardiovasc Interv. 2004; 63(4): 496–502, doi: 10.1002/ccd.20211, indexed in Pubmed: 15558755.

12. Rodés-Cabau J, Mineau S, Marrero A, et al. Incidence, timing, and predictive factors of new-onset migraine headache attack after transcatheter closure of atrial septal defect or patent foramen ovale. Am J Cardiol. 2008; 101(5): 688–692, doi: 10.1016/j.amjcard.2007.10.034, indexed in Pubmed: 18308022.
13. Fernandes-Mayorales MD, Fernandez-Jean A, Munoz-Jareno N. Migraine symptoms related to the percutaneous closure of an ostium secundum atrial septal defect: report of four pediatric cases and review of the literature. Cephalalgia. 2007(27): 550–556, doi: 10.1111/j.1468-2982.2007.01331.x, indexed in Pubmed: 17459082.
14. Białkowski J, Szkutnik M. The use of Amplatzer devices in the percutaneous treatment of congenital heart defects in children and adults based on own experience. Kardiol Pol. 2021; 79(10): 1130–1132, doi: 10.33963/KP.a2021.0092, indexed in Pubmed: 34403488.
15. Feltes TF, Bacha E, Beekman RH, et al. Indications for cardiac catheterization and intervention in pediatric cardiac disease: a scientific statement from the American Heart Association. Circulation. 2011; 123(22): 2607–2652, doi: 10.1161/CIR.0b013e31821b1f10, indexed in Pubmed: 21536996.
16. Ries MW, Kampmann C, Rupprecht HJ, et al. Nickel release after implantation of the Amplatzer occluder. Am Heart J. 2003; 145(4): 737–741, doi: 10.1067/mhj.2003.7, indexed in Pubmed: 12679773.
17. Wallace S, Dohlen G, Holmstrom H, et al. Cerebral microemboli detection and differentiation during transcatheter closure of atrial septal defect in a pediatric population. Cardiol Young. 2014; 25(1): 1–8, doi: 10.1017/S1047951113002072, indexed in Pubmed: 24522121.
18. Carlson KM, Justino H, O'Brien RE, et al. Transcatheter atrial septal defect closure: modified balloon sizing technique to avoid overstretching the defect and oversizing the Amplatzer septal occluder. Catheter Cardiovasc Interv. 2005; 66(3): 390–396, doi: 10.1002/ccd.20443, indexed in Pubmed: 16142805.
19. Wilmshurst PT, Nightingale S, Walsh KP, et al. Clopidogrel reduces migraine with aura after transcatheter closure of persistent foramen ovale and atrial septal defects. Heart. 2005; 91(9): 1173–1175, doi: 10.1136/hrt.2004.047746, indexed in Pubmed: 16103551.
20. Hascoet S, Hadeed K, Marchal P, et al. The relation between atrial septal defect shape, diameter, and area using three-dimensional transoesophageal echocardiography and

balloon sizing during percutaneous closure in children. Eur Heart J Cardiovasc Imaging. 2015; 16(7): 747–755, doi: 10.1093/ehjci/jeu316, indexed in Pubmed: 25617028.

Table 1. Baseline characteristics of the patients and procedures. Data presented as median (interquartile range [IQR]) or percentage value

Variable		**THE (+) n = 40**	**THE (-) N = 800**	*P*
Female sex		n = 28 (70%)	n = 571 (71%)	
Age, years		13 (7.35–16)	5 (3–10)	<0.001
Weight, kg		45 (22.4–54.5)	19 (14–37)	<0.001
BC, %		82.5% n = 33	43.3% n = 344	<0.001
Balloon waist, mm		19 (16–22)	15 (12–18)	<0.001
Device waist/ASD diameter, mm		6 (3–8)	3 (2–5)	<0.001
Device, mm		18 (13.5–22)	14 (11–17)	<0.001
Residual shunt, %	24 h	12.5% n = 5	4.9% n = 39	0.03
	1 y	7.5% n = 3	1.0% n = 8	<0.001
ASD diameter in TEE, mm		12 (8–14.5)	10 (8–13)	0.19
Fluoroscopy time, min		3 (2–5)	3.1 (2.2–5)	0.78
Nickel release protection, %		5% n = 2	33.3% n = 264	<0.001

Abbreviations: ASD, atrial septal defect; BC, balloon calibration; THE, transient headache episodes; TEE, transesophageal echocardiography

Table 2. Predictors of THE occurrence in the regression model.

Variable	**Odds ratio (95% CI)**
Age	1.18 (1.09–1.27)
Nickel release protection	0.13 (0.03–0.58)
Fluoroscopy time	0.91 (0.83–0.1)
Use of balloon calibration	3.68 (1.43–9.48)
Oversizing (Device size/ASD diameter ratio)	1.09 (1.01–1.19)

Abbreviations: see Table 1

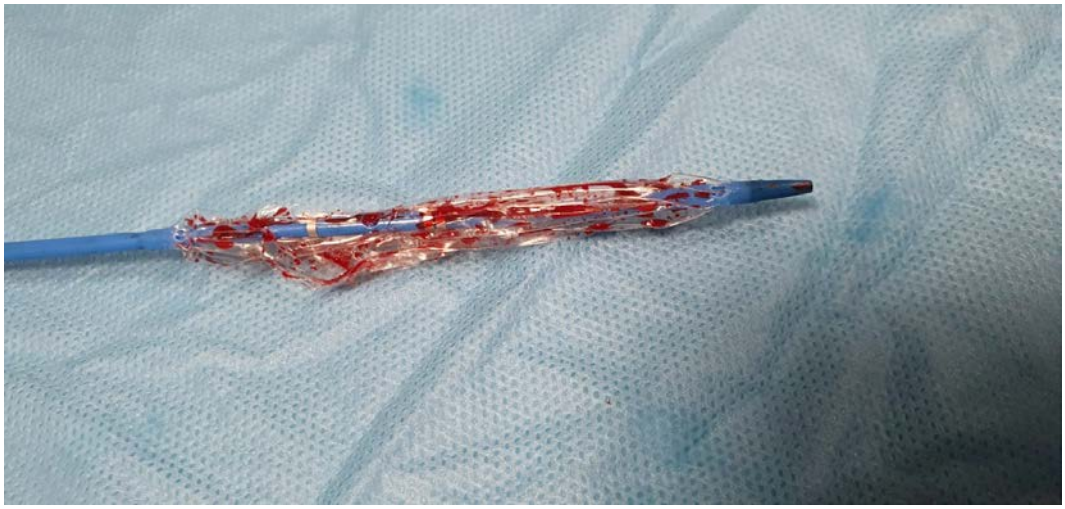

Figure 1. Numerous micro-clotting on balloon surface present despite adequate heparinization

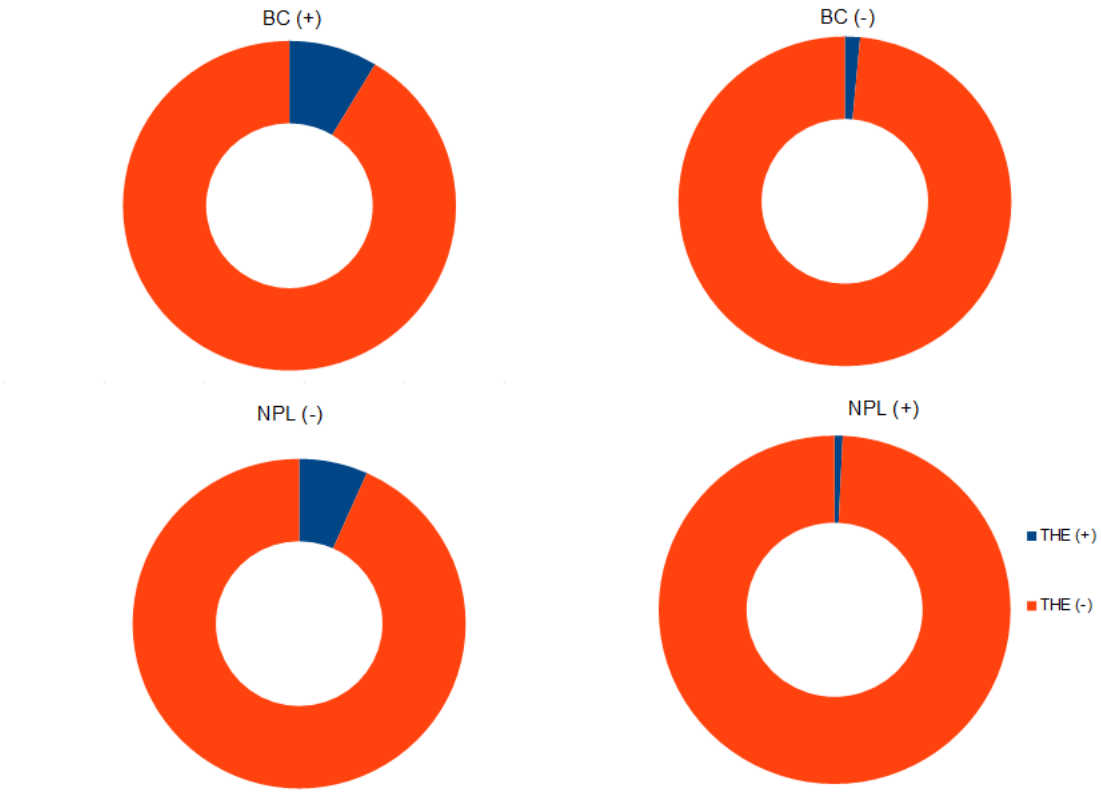

Figure 2.

Abbreviations: BC, balloon calibration; NPL, nickel protection layer; THE, transient headache episodes