ABSTRACT

INTRODUCTION: There are no recent estimates of the complication rate associated with Intra Arterial Heparin Flushing (IAHF). The purpose of this study was to estimate the rate of complication occurring during and after Intra Arterial Heparin Flushing.

METHOD: This report is a descriptive study based on analysis of interventional radiology database. The study involved patients who underwent IAHF procedure started from January 2018 until December 2018 in Rumah Sakit Pusat Angkatan Darat Gatot Soebroto (Indonesian Army Central Hospital). Subjects were assessed for their age, sex, medical history, diagnosis, intra-procedural complication, and post-procedural complication.

RESULT: All IAHF procedures were performed via transfemoral catheterisation and using a vascular closure device to help achieve homeostasis. Our population included 1223 (70.57%) male and 510 (29.43%) Female, with age ranging from 21 to 80 years old. The majority of the subject was in 51-60 years old age group (35.31%). All IAHF were technically successful. No intraprocedural complication was noted, there was no occurrence of iatrogenic vessel injury (dissection) and no neurological deficit secondary to IAHF procedures. There was some local complication after IAHF procedure such as hematoma 44 persons (2.54%), oedema around the puncture site six patients (0.35%), and bleeding at the puncture site three patients (0.17%). Beside local complication, there were several systemic complications such as allergy in 10 persons (0.58%). No neurological complication was reported after IAHF.

CONCLUSION: We concluded that IAHF has a relatively low rate of acute complication. Most complications were related to local hemostasis control, and no severe sequelae were found.

INTRODUCTION

Digital Subtraction Angiography is a procedure to visualise blood flow inside the brain vessels. It is essentials for the diagnosis and treatment evaluation of cerebrovascular disorder as it provides hemodynamic information related to brain anatomical structures.1 In early years of angiography, a technique that relies on X-ray imaging and iodinated radiopaque contrast agent that injected into the bloodstream.2 However, angiography technique has been improved and benefited significantly from the invention of cross sectional imaging and advance in digital computation, leading to digital subtraction angiography. DSA, in addition to providing the vascular image, it allows for the unwanted elements to be removed by image subtraction.3 Currently, DSA is more widely accepted in the diagnosis, treatment planning and evaluation of neurovascular pathology.3

Fluoroscopically guided interventional procedures with digital subtraction angiography (DSA) are being performed with increasing frequency as diagnostic of choice for a variety of neurovascular diseases as the prevalence of cerebrovascular disease increase over time.4 It is currently the most accurate imaging technique for evaluation of the cerebrovascular system.4,5 In this technique, an injection of contrast agent, is conducted, then follow by monitoring the contrast arrival into the brain circulation by the acquisition of a C-arm.4

Endovascular procedures such as DSA would be risky without inhibition of the coagulation cascade. Synthetic surfaces of catheters and wires are thrombogenic. Besides, tissue damage from vessel punctures, sutures, and angioplasty exposes tissue factor which acts as the trigger for coagulation.7 The use of heparin during interventional procedures, both as a bolus or diluted with saline to flush catheters has practised, and heparin antithrombotic properties hold an indispensable role for most interventional procedures.8,9,10

Intra Arterial Heparin Flushing (IAHF) is a modification of Digital Subtraction Angiography (DSA) that works for both diagnostic and therapeutic procedure. Its extensive descriptions were

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published across many studies by Terawan et al. Principally, it uses the unfractionated heparin applied directly to the site of vascular occlusion through a catheter. Heparin not only an anticoagulant but also a fibrinolytic because it can increase plasminogen conversion into plasmin by stimulating plasminogen activator. There is still no recognised consensus among the profession of a preferred concentration of heparinised saline, heparin bolus dose and its timing. Due to its effects, Heparin have common side effect including haemorrhage, hematoma, and prolonged compression time to stop bleeding.

There are two possible ways to achieve hemostasis of the access puncture site after intervention procedure, manual compression (MC) or insertion of a vascular closing device (VCD). Vascular closure device that we used at the end of the IAHF procedure followed by 4 hours of patient immobilisation. It used to achieve hemostasis after procedures requiring percutaneous common femoral artery puncture. VCD reliably shortens the time to hemostasis compared with manual compression and thus allows earlier patient ambulation. Manual compression usually requires sustained partially occlusive pressure over the arterial access site for approximately 15–20 minutes, followed by 6-8 hours of patient immobilization.

The complications of conventional cerebral angiography have been studied in many centres and were the subject of a recent review. However, there was no report related to the complication of the IAHF procedure.

**METHODS**

This report is a descriptive study based on analysis of interventional radiology database approved by our institution. Retrospective analysis of patient, procedural characteristics and complication were conducted. All IAHF procedures were performed based on accepted clinical indications for treatment. This study involved patients underwent IAHF procedure started from January 2018 until December 2018 in Rumah Sakit Pusat Angkatan Darat Gatot Soebroto (Indonesian Army Central Hospital). All IAHF procedures were performed via the femoral artery approach and used a vascular closure device to achieve hemostasis. The procedure performed at a time was only IAHF with local anaesthesia and without any other interventional radiology procedure such as cardiac angiography, coiling, venography, etc. Subjects were assessed for their age, sex, medical history, diagnosis, intra-procedural complication, and post-procedural complication. The exclusion criteria for the study included severe peripheral vascular disease, aged less than 21 or more than 80 years old, patient treated with IAHF procedure with another interventional procedure.

All the IAHF procedure was performed by a staff of interventional radiologist in RSPAD Gatot Soebroto. The IAHF technique started from the application of topical Eutectic Mixture of Local Anesthetics (EMLA) on the planned femoral artery puncture site, continued with puncture site decontamination with povidone-iodine 7.5% and alcohol 70%. Local anaesthetic (Lidocaine) was injected intracutaneously and subcutaneously. While waiting for the local anaesthetic action, 5000 IU heparin was diluted with 500 mL normal saline. The femoral artery was punctured with intravenous cannula 18 G, and a short guidewire was inserted and followed by catheter insertion and navigation to desired site while fluoroscopy was performed to see the anatomical image. Diluted heparin was flushed intraarterially in both right and left carotid arteries and vertebral arteries. After completing the flushing process, femoral artery bleeding was stopped using vascular closure device.

Subjects were monitored on a flatbed at the wards for 4 hours after hemostasis. Vital sign measured as soon as the subjects back to the ward and before discharge from hospital. Subjects who were discharged underwent neurologic examination performed by neurologist and puncture site examination performed by the interventional radiologist.

**RESULT**

The data for this review consisted of consecutive IAHF procedure performed in 1733 patients. The studied sample includes 1223 (70.57%) males and 510 (29.43%) females with age ranging from 21 years to 80 years. The majority of the patients were in the 51-60 years old age group, which consisted of 612 subjects (35,31%). Overall, the patient has multiple medical histories and the most common was uncontrolled hypertension (41.03%). Table 1 also shows medical history and demography for IAHF procedure, and indication for IAHF are outlined in Table 2.

The clinical indication for the procedure was 667 (38,49%) persons with chronic stroke (infarct), 1038 (59,90%) persons with cerebral venous thrombosis and 28 (1,61%) persons with other neurological diseases (Table 2).

All of the IAHF procedures were technically successful. The mean total time for IAHF procedure was 30 minutes. No intraprocedural complication was noted. There was no occurrence of iatrogenic vessel injury. Therefore, the rate of intraprocedural complications was 0,0%.
There was post-procedural complication noted occurring 4 hours after IAHF procedure. Recorded complications were divided into three groups: Local, Systemic, and Neurologic. Among the 1733 patients underwent IAHF procedure, local complication reported, such as hematoma, oedema around the wound, and bleeding at the procedural site. All the local complication was reported in table 3. The hematoma was reported in 44 patients (2.54%). After 4 hours monitoring in the ward, oedema around puncture site was reported in 6 patients (0.35%), three patients (0.173%) was reported bleeding at the procedural site after the patients attempted an early mobilisation (<4 hours).

Besides the local complication, there was systemic complication such as nausea and vomiting reported in 3 patients (0.17%) and allergy was reported in 10 patients (0.58%). Another neurologic complication such as headache was reported in 2 patients (0.11%), but there was no neurologic deficit reported in the first 4 hours post-IAHF procedure.

Some patients experienced more than one complication. The most common complications observed after IAHF procedures (bleeding at the puncture site and hematoma at the puncture site) are those commonly associated with headache history and patients attempted movements before 4 hours post-IAHF procedure with a vascular closure device.

All complications were recognised and treated accordingly in the ward during monitoring or immediately following the examination within 4 hours after the IAHF procedure for the closure device group.

### DISCUSSION

Our retrospective review among 1733 IAHF procedure reveals relatively low complication rates. Hematoma at the puncture site was found in 2.54% of patients and was the most common complication. In this context, the hematoma is defined as a collection of blood within the soft tissues of the upper thigh. It can be associated with the profiles of the catheters sheaths and indirectly implicated to the length of stay. The development of vascular closure devices has improved patient comfort and could reduce the occurrence of local hematoma and bleeding complications.

Another study reported that walking was possible within 7.2 ± 2.7 hours after hemostasis with a compression device and 17.3 ± 4.3 hours after manual hemostasis. Recently, patients have been able to walk within 4-5 hours, and the discomfort of patients caused by lengthy bed rest and lengthy hospitalisation period has been reduced using the vascular closure device. Vascular closure device was increasingly being used in the patient after the IAHF procedure. We prefer the use of a vascular closure device for all patients because it can improve
These patients had a positive headache history before the procedure, migraine in particular. Half of patients undergoing routine angiography experience benign post-procedure headaches within 24 h (especially women).

In conventional cerebral angiography, positioning a catheter in a potentially diseased vessel, there is a risk of thrombotic material at the catheter tip or dislodge atheromatous material from the diseased vessel wall, embolizing and causing neurologic complications. We found headache after IAHF procedure in 0.17% from 1733 procedure, but it improved after the patients have rehydrated without any analgesic. Based on the previous study, headache is a common symptom after cerebral angiography, although it has seldom been studied. We aimed to evaluate the frequency of headache at 24 h and 6 months after angiography and to describe its characteristics. We used a cross-sectional survey of consecutive patients submitted to angiography and determined headache presence and its characterization. Headache occurrence was analyzed against headache history, clinical data, technical and demographical variables. Of 107 procedures studied, 51.3% patients experienced headaches within 24 h. Patients more likely to experience headaches were females or had subarachnoid hemorrhage. Six months post-procedure 48.8% of patients had frequent headaches. These patients had a positive headache history before the procedure, migraine in particular. Half of patients undergoing routine angiography experience benign post-procedure headaches within 24 h (especially women).

Another complication like allergic reaction after IAHF procedure caused by contrast media. All contrast agents are based exclusively on iodine. It combined to a benzoic acid ring in a mixture of meglumine or sodium salt of diatrizoate acid with calcium EDTA. In order to achieve the iodine concentration that is needed for optimal visualisation during angiography, solutions of conventional contrast agents were extremely hypertonic. We used iodixanol as a contrast for IAHF procedures because iodixanol is safe and more tolerated in the injection phase with superior contrast enhancement and lesion distinction. It has the same osmolarity with blood (290 mOsm/kg). From all IAHF procedures, we found only 0.58% from 1733 patient had allergy with contrast. The allergies were presented as redness, itchy, or swollen at the eyes. However, there was not reported any anaphylactic reaction in this report. Likewise, there are two categories of patients at risk for anaphylaxis that should be considered for pre-treatment. The first is patients with previous anaphylactic reactions that are at the highest risk for developing recurrent reactions. The second is patients with history of atopy, asthma or those who take beta-adrenergic blockers, in whom a twofold risk in anaphylaxis has been reported.

We realise that there were potential limitations in our study. The data accuracy depended very strongly on the reliability of our clinical follow up in 4 hours after the IAHF procedure. The nature of this retrospective study design also has limitations. Further study with specific aims and design should be conducted in the future to evaluate a more detailed aspect of IAHF.

CONCLUSION

The result of our study showed a relatively low rate of acute complication of IAHF procedure. Most
complications were related to local hemostasis control, and no severe sequelae were found.

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All authors have contributed to all process in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest regarding the publication of this article.

REFERENCE