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ORIGINAL RESEARCH

Comparison of normal saline and heparinized solutions for the maintenance of arterial catheter pressure waves: a randomized pilot study

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Abstract

Objectives: Heparinized continuous-flush solutions are used to maintain arterial catheter patency. We sought to compare the patency and pressure wave integrity of radial artery catheters maintained with heparinized or nonheparinized infusions. **Methods**: Patients in the emergency room and intensive care unit were consecutively enrolled and randomly assigned to receive a heparinized solution (heparin group, n = 18) or normal saline (NS group, n = 16). The functional duration of radial artery catheters, the differences between arterial catheter and brachial cuff blood pressures, and the pressure wave curve quality were determined. **Results**: The mean duration of functional cannulas did not differ significantly between the heparin and NS groups (120 $\pm$ 129 and 105 $\pm$ 82 hours, respectively, P = 0.689). There was no difference in blood pressure between arterial catheter measurements and brachial cuff measurements between the two groups (P = 0.607). Kaplan-Meier analysis showed that the incidence of pressure wave dampening did not differ between the groups (log-rank test, P = 0.896). **Conclusions**: No significant differences were found between heparinized and nonheparinized flush solutions for maintaining radial artery catheter patency and function.

Keywords

Heparin; Intensive care; Emergency room; Catheter; Blood pressure monitoring

1. Introduction

Arterial catheters are used for not only blood pressure monitoring but also for cardiac output measurements with an arterial pressure-based cardiac output measurement (APCO) device [1]. An APCO device allows determination of the stroke volume based on arterial waveform characteristics. Since the APCO device may replace the pulmonary arterial catheter-based thermodilution method, their importance increases in the emergency rooms and cardiac intensive care units [2]. Because APCO devices are simple and non-invasive, they are becoming a popular device for circulatory monitoring of critically ill patients with or without cardiovascular disease in the emergency room and intensive care unit (ICU) settings.

For decades, the patency of arterial catheters has been maintained with a pressurized and continuous infusion of heparin to reduce thrombus formation [3]. Whether a heparinized solution can maintain arterial catheter patency and what concentration of heparin is recommended to prevent loss of patency has been debated [4]. Despite its increased use, the benefit of heparin for arterial waveform maintenance has not been established. Utilization of a heparinized solution to maintain the patency of an arterial catheter carries some risks. Heparin therapy can produce severe complications such as heparin-induced thrombocytopenia (HIT) in 0.5%-5% of patients [5, 6], and can affect the results of coagulation studies if blood samples are drawn from the arterial catheter [7].

Many previous studies have aimed to determine the patency of arterial catheters and the incidence of complications [8]. In order to obtain accurate measurement of blood pressure and stroke volume with an arterial catheter, catheter patency and the integrity of the arterial waveform should be maintained. Few previous studies have evaluated the association between maintenance of the arterial waveform and heparinized solutions [9]. We undertook this study to evaluate whether heparin is necessary to maintain the integrity of arterial waveforms with an arterial catheter and to determine whether the failure rate of an arterial catheter differs depending on whether a heparinized or nonheparinized infusion solution was used.

2. Materials and methods

This study was approved by the Tokyo Medical University Institutional Review Board (IRB approval no. 2042). This study conformed to the tenets of the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013).

2.1 Participants

This randomized, controlled, single-blinded clinical trial included all adult critically ill patients who visited the Department of Emergency and Critical Care Medicine of Tokyo Medical University Hospital between July 2012 and December 2012. Our department is a tertiary emergency care center consisting of an emergency room (ER) and a 20-bed mixed ICU for medical and surgical patients. Approximately 1,500 patients were treated in the department in 2012.

Written informed consent was obtained from each patient or from the guardian prior to enrollment in the study. Patients having a 22-gauge polyurethane intravascular catheter (Insyte™, Becton, Dickinson and Company, Tokyo, Japan) placed in the radial artery were included in the study. Inclusion criteria were an age of $>$ 18 years, provision of informed consent, catheter retention for at least 6 hours, and placement of a single arterial line. Exclusion criteria were a history of heparin allergy, preexisting coagulopathy, and failure to provide informed consent.

2.2 Interventions

Cannulation was performed with the maximal barrier precaution technique [10]. The catheter was connected to an arterial line, which consisted of a standard arterial flush system connected to an arterial pressure monitoring circuit. The delivery system for the flush solution was prepared using a 500-mL NS bag pressurized to 300 mmHg and delivered as a continuous flush at a rate of 3 mL/h.

Patients were randomly assigned to one of two groups. Patients in the heparin group received a flush solution containing 2 U/mL heparin with 0.9% sodium chloride via the arterial line. Patients in the NS group received a flush solution containing only sodium chloride. Random numbers were placed into sealed envelopes, which were opened before preparation of each arterial line.

The sample size was determined based on a previous study [11]. However, since the sample was small, we decided to conduct this as a pilot study.

2.3 Measurements

We reviewed patient demographic and clinical characteristics from hospital records. The length of time (in hours) that the arterial catheter was functional was documented. The reasons for catheter removal were as follows: assessment as clinically unnecessary by the physician, catheter failure, and accidental removal by the patient. The pressure gap, which was calculated as the mean blood pressure measured with the arterial line minus the pressure measured with the brachial cuff, was recorded before catheter removal. Registered nurses evaluated catheter failure; assessed the ability to remove blood using a syringe and the integrity of waveforms with normal morphology. The functional life span of the arterial catheters was determined by the quality of the pressure waveforms. Before catheter removal, a blood sample was taken to determine the activated partial thromboplastin time (APTT). The measured value was divided by the control value to calculate the APTT ratio. After catheter removal, a blinded investigator assessed the patient for infection and hematoma at the puncture site.

2.4 Statistical analysis

Descriptive analysis was performed using percentages for categorical variables and means with standard deviations for continuous variables. Comparisons were performed using the chi-squared test for categorical variables and Welch's t test for continuous variables. The functional life span of the arterial catheters was evaluated using the Kaplan-Meier method at removal, and data were statistically compared using the log-rank test. Statistical analyses were performed using the BellCurve for Excel software (Social Survey Research Information Co., Ltd., Version 3.20). A P value of < 0.05 was considered a statistically significant difference.

TABLE 1. Demographics and clinical characteristics of the patients.

	Heparin (n = 18)	NS (n = 16)	P value
Age	70.7 ± 16.4	68.6 ± 20.6	0.739
Sex (female/male)	5/13	7/9	0.331
Other anticoagulant use	1	1	0.932
Diagnosis			
Medical	14	12	0.849
Trauma	3	3	0.874
Exogenous disease	1	1	0.932

The values are presented as means ± SDs or as numbers.
NS: normal saline group.

3. Results

A total of 34 patients were enrolled. Eighteen patients received heparinized flush solution (heparin group), and 16 received NS without heparin (NS group) (Fig. 1). The demographic and clinical characteristics of the patients are shown in Table 1. The patients in the heparin and NS groups were well matched with respect to age and sex ($P > 0.05$). The mean duration of cannulation did not differ significantly between the heparin group and the NS group (120 ± 129 and 105 ± 82 hours, respectively, $P = 0.689$) (Table 2). In addition, the gap in blood pressure between that measured with the arterial line and that measured with a brachial cuff did not differ significantly between the two groups ($P = 0.607$). The volume of flush solution used between the groups was nonsignificant ($P = 0.650$). The APTT did not differ significantly between the heparin group and the NS group ($P = 0.689$). The incidence of catheter obstruction and arterial pressure waveform deterioration were similar between the groups (Table 3). Kaplan-Meier analysis showed no differences in the incidence of pressure wave dampening between the groups ($P = 0.896$, Fig. 2). The incidence of hematoma after catheter removal was similar between the two groups, and no infections were observed at the puncture sites.

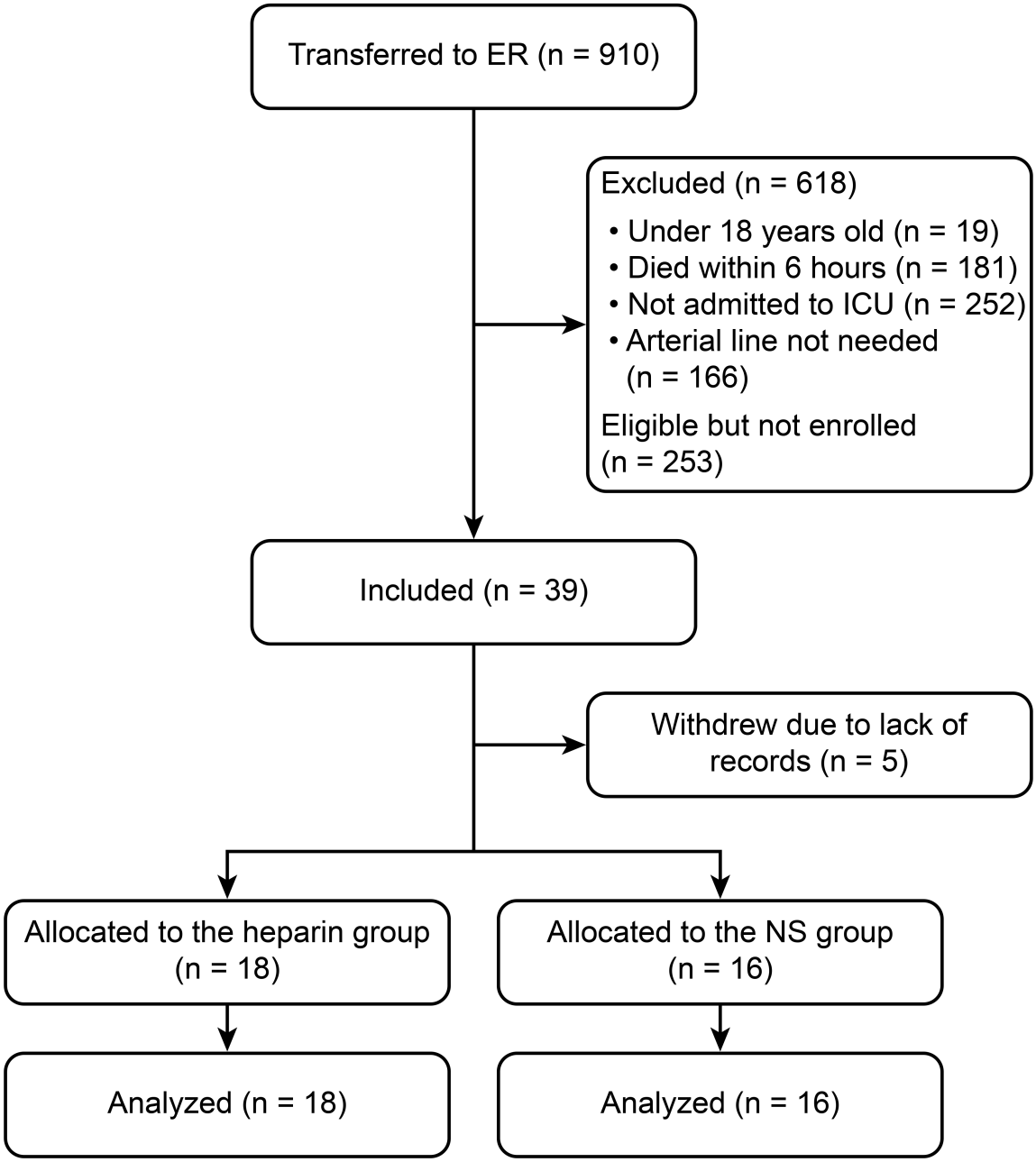

FIGURE 1. Trial flowchart. ER: emergency room; ICU: intensive care unit.

TABLE 2. Main variables in the study.

	Heparin (n = 18)	NS (n = 16)	*P* value
Mean duration of cannulation (h)	120 ± 129	105 ± 82	0.689
Gap in blood pressure (mmHg)	2.6 ± 24	11 ± 29	0.607
APTT (ratio to control)	1.01 ± 0.16	1.03 ± 0.16	0.689
Flush solution volume (mL/h)	3.5 ± 2.5	4.1 ± 3.6	0.650

The values are presented as means ± SDs or as numbers.
NS: normal saline group.
APTT: activated partial thromboplastin time.

4. Discussion

In this study of 34 patients in the mixed medical and surgical emergency care center, we found no difference in the functional life span between radial arterial catheters continuously flushed with 2 U/mL heparin solution vs. a nonheparinized NS solution. Arterial catheters are used for both continuous blood pressure monitoring and cardiac output measurement in acute care. Arterial catheters also provide continuous access for blood sampling, thus decreasing patient discomfort

TABLE 3. Complications and adverse events.

	Heparin (n = 18)	NS (n = 16)	*P* value
Catheter obstruction	2	2	0.844
Deteriorating waveform	7	7	0.882
Hematoma	1	2	0.906

The values are presented as means ± SDs or as numbers.
NS: normal saline group.

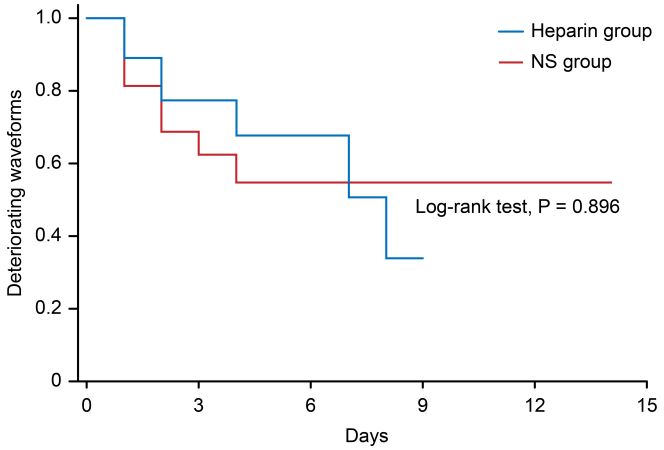

FIGURE 2. Kaplan-Meier curves of deteriorating waveforms. The vertical axis shows the percentage of the integral waveform, and the horizontal axis shows the number of days after insertion. *P* = 0.99 with the log-lank test. The red line indicates the heparin group. The black line indicates the NS group. NS, normal saline.

from repeated venous or arterial punctures. The anticoagulant properties of heparin led clinicians to use heparin flushes or heparinized infusions in an attempt to prevent thrombus formation and to prolong the duration of catheter patency. The French Society of Anesthesia and Intensive Care guidelines for arterial catheterization in adults has recommended the addition of heparin for catheters in place for more than 24 hours [12].

Various studies have compared the effect of heparinized and NS solutions on arterial catheter patency. Clifton *et al.* [11] found that there were significant differences in favor of heparin. The duration of catheterization in the heparin group was longer than that in the NS group. However, the percentage of functional catheters in the NS group was decreased (only 52% after 40 hours). Zevola *et al.* [13] showed that arterial catheters failed less often when maintained with heparinized solutions and that failure occurred in 42.9% of patients in the no-heparin group. In the current study, catheter obstruction occurred in 12.5% of the patients in the NS group; which was not significantly different from the heparin group. The low incidence of catheter failure in the NS group may have been dependent on improvements in device setup and maintenance of arterial catheters established in recent ICU care protocols. In our ICU, nurses checked the arterial catheter waveform and whether the catheter was in the correct position every two hours. The nurses also performed device setup twice a day routinely. In a recent review, Kordzadeh *et al.* [14] showed that there was a significant effect on heparin when arterial catheters were used for longer than 48 hours. Furthermore, with the advent of new devices in recent years, it is also important to maintain the waveform of the arterial catheter. Few studies have shown an association between heparin and maintenance of arterial catheter waveform. Alizadehasl *et al.* [9] concluded that there was no significant difference between heparinized solution and normal saline for maintenance of arterial catheter waveform. In our study, in which the arterial catheters were in place longer than the study of Alizadehasl *et al.* [9], we also found no significant difference for waveform maintenance between heparinized solution and normal saline.

The optimal concentration of heparin in the flush solution has been another topic of discussion. Early studies had a tendency to use higher heparin concentrations [11, 13]. In a study by Branson *et al.* [15], 4 U/mL heparin was necessary in the flush solution to extend the catheter life span. Butt *et al.* [16] compared the effectiveness of 5 U/mL and 1 U/mL heparin in a clinical trial conducted in children. They showed that an increase in heparin concentration from 1 to 5 U/mL prolonged the patency of the arterial catheter. In a more recent trial, 4 U/mL heparin was considered much higher than that the commonly used concentrations [7]. In accordance with current practice, we used 2 U/mL heparin in the standard flush solution in the ICU. However, adverse effects of heparin may occur even at low doses [17]. It has been reported that small amounts of heparin may result in HIT [18, 19].

The addition of heparin to the flush solution has not been shown to increase arterial catheter patency compared to NS. Switching to NS as the flush solution can maintain catheter patency and reduce the risk of developing HIT. In addition, switching to NS may also reduce hospital costs. Although permanent ischemic damage to the hand after radial artery cannulation is rare, the potential for ischemic damage resulting from radial artery occlusion during or after cannulation is an important concern. Moreover, the incidence of arterial thrombosis is correlated with the presence of hematoma at the puncture site [7]. In a recent review, Robertson-Malt *et al.* [8] suggested that heparin 1-2 U/mL and saline were equally effective in maintaining the patency and function of arterial catheters. On the other hand, Kordzadeh *et al.* showed that higher heparin levels have a higher incidence of arterial catheter patency. In this study, local subcutaneous hematoma was observed in only a few patients. Therefore, heparin did not contribute to the prevention of postcannulation ischemic changes.

This study has some limitations. First, the sample size was small, suggesting a lack of statistical power to detect small differences between the groups. Therefore, we have conducted this study as a pilot study. Second, the nurses who changed the pressurized bags with the flush solution were not blinded to the contents of the bag. Finally, we did not adopt objective criteria or tests to evaluate dampening of pressure waves in the arterial lines. This assessment was carried out mainly by visual assessments during routine daily care.

5. Conclusions

We may conclude that heparin flush solutions do not affect the function or duration of radial arterial catheters used for blood

pressure monitoring. A larger study, adequately powered to detect differences in arterial catheter patency, wave form analyses, and complications is needed to further define the role of heparin flush solutions in clinical practice.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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