



## Comparison of Arterial Line Patency in Heparinized Normal Saline with Normal Saline Flushing Among Critically ill Patients: A Literature Review

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### ABSTRACT

Hemodynamic monitoring in critically ill patients is often invasive, using an arterial line. The monitoring accuracy is highly dependent on the patency of the arterial line, which is often compromised by artery blockages. So far, heparin in normal saline is believed to prevent these complications compared to normal saline alone. This study aimed to compare the effectiveness of normal saline flushing with heparin with normal saline use on arterial line patency. The method of the study was a review. Keywords were compiled using words such as critical care unit, heparinized saline, normal saline, and arterial line patency with boolean operators. Searched extensively through PubMed, Science Direct, and Google Scholar, Data were analyzed using the extraction table and presented with qualitative analysis. The initial search identified 370 articles. Seven articles were obtained after being selected through the duplication, title, abstract, and inclusion-exclusion criteria. All articles mentioned that there was no significant difference between the use of normal saline added with heparin with normal saline on arterial line patency. Based on the study, it can be concluded that the use of normal saline alone as an arterial line flush is recommended because it reduces the risk of Heparin-Induced Thrombocytopenia, allergy to heparin, bleeding and is economically more cost-saving.

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### Kata kunci:

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### ABSTRAK

Pemantauan hemodinamik pada pasien kritis seringkali dilakukan secara invasif, menggunakan jalur arteri. Keakuratan pemantauan sangat tergantung pada patensi *arterial line*, yang seringkali terganggu oleh penyumbatan arteri. Sejauh ini, heparin dalam salin normal diyakini dapat mencegah komplikasi tersebut dibandingkan dengan pemberian normal salin saja. Penelitian ini bertujuan untuk membandingkan efektivitas *flushing* menggunakan normal saline ditambah heparin dengan penggunaan normal salin terhadap kepatenan *arterial line*. Penelitian ini merupakan literatur *review*. Kata kunci dikompilasi menggunakan *critical care unit*, *heparinized saline*, *normal saline*, dan *arterial line patency* yang dikombinasikan menggunakan *boolean operator*. Hasil-hasil penelitian dicari secara ekstensif melalui PubMed, Science Direct, dan Google Scholar, data dianalisis menggunakan tabel ekstraksi dan disajikan menggunakan analisis kualitatif. Pencarian awal berhasil mengidentifikasi 370 artikel. Tujuh artikel kemudian diperoleh setelah melalui seleksi menggunakan kriteria duplikasi, judul, abstrak, dan inklusi-eksklusi. Semua artikel menyebutkan bahwa tidak ada perbedaan yang signifikan antara penggunaan

normal saline ditambah heparin dengan normal saline terhadap kepatenan *arterial line*. Berdasarkan penelitian dapat disimpulkan bahwa penggunaan *flushing* menggunakan normal saline saja direkomendasikan karena mengurangi risiko trombositopenia yang diinduksi heparin, alergi terhadap heparin, perdarahan dan dilihat dari biaya, lebih ekonomis

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## INTRODUCTION

In the Intensive Care Units (ICU), hemodynamic monitoring is crucial for critically ill patients. Invasive hemodynamic monitoring may provide continuous monitoring results with a higher accuracy level, so invasive methods are believed to have better advantages than non-invasive methods (Langwieser et al., 2015). Although invasive hemodynamic monitoring is more expensive, riskier (Leslie et al., 2013), and requires more capability in installation and monitoring than non-invasive monitoring, this method has been accepted as a standard method in monitoring critically ill patients (Miller et al., 2014).

In post-cardiac surgery or critical patients requiring close hemodynamic monitoring, an arterial line is usually placed to monitor systemic blood pressure and routine blood tests accurately. Furthermore, the monitoring accuracy is highly dependent on the patency of the arterial line (Alizadehasl et al., 2015; Heidari et al., 2015). However, the installation of an arterial line cannot be separated from a variety of complications (Chim et al., 2015). Complications that may occur are improper arterial waveform, bleeding, hematoma, arterial line occlusion, tissue ischemia, infection, and, most importantly, arterial thrombosis (Brancati et al., 2012; Goossens et al., 2013; Handlogten et al., 2014; Rawlins et al., 2006).

For decades, arterial line patency has been maintained by continuous infusion of heparin in normal saline with positive pressure to reduce thrombus formation and blood return. Despite its frequent use, the advantage of heparin in maintaining arterial line patency and the concentration levels recommended to prevent loss of patent are still being debated (Kordzadeh et al., 2014). Several studies have shown that continuous use of heparin, even in small doses, may cause thrombocytopenia and bleeding (Bertoglio et al., 2012; Brzezinski et al., 2009; Warkentin et al., 2013). On the other hand, a review by Kordzadeh et al. (2014) stated that flush solution heparin at higher doses and continuous infusion had a better incidence of patency in the absence of reports of Heparin-Induced Thrombocytopenia (HIT). However, a review by Kordzadeh et al. (2014) showed different results from recent studies.

Recent evidence suggests that normal saline can maintain arterial line patency, increase the accuracy of coagulation tests, and prevent patients from being affected by heparin-induced complications (Alizadehasl et al., 2015; Robertson-Malt et al., 2014; Tamura et al., 2021; Xiong et al., 2019). However, it should be considered that normal saline does not have anti-coagulation properties, so catheter patency, vascular thrombosis, tissue damage, and infection are still concerns (Everson et al., 2016). Thus, it was necessary to determine whether the benefits of heparin outweigh the potential risks compared to normal saline as a flush fluid for arterial lines (Robertson-Malt et al., 2014).

Nurses have a significant role in the implementation of hemodynamic monitoring. The nurse observes the patient's

hemodynamic condition closely for twenty-four hours to anticipate if a problem occurs immediately. Furthermore, arterial line patency determines the accuracy of systemic blood pressure, one of the emergency predictors. Consequently, nurses need to maintain arterial line patency. Based on those considerations, the authors were interested in conducting a literature review comparing heparin flush in normal saline with normal saline in arterial line care to maintain patency of arterial line for hemodynamic monitoring in the adult ICU patient population.

## METHODS

### *Research design*

This study used a descriptive literature review method to identify the effectiveness of arterial line patency given heparin flush with normal saline compared to normal saline flush alone. The research questions were developed based on the PICO. The population in this review were adults with arterial line insertion who used normal saline flush with heparin at any dose compared to normal saline without heparin. Flush should be given continuously by infusion (usually a pressure of 300 mmHg to achieve a constant infusion rate of 3cc/hour). Outcomes assessed were the patency or duration of arterial line use and the presence or absence of unexpected events (arterial line blockage, bleeding, thrombocytopenia).

### *Search methods*

Search articles used three electronic databases, including PubMed, ScienceDirect, and Google Scholar, with the keywords critical care unit, heparinized saline, normal saline, and arterial line patency. The Boolean operators 'OR' and 'AND' were used in the literature search.

### *Eligibility criteria*

The inclusion criteria in the literature search were articles published in English in the 2011-2021 range (last 10 years), and original articles. In addition, the exclusion criteria were articles with qualitative methods, literature/systematic reviews, book chapters, and literature that did not meet the research objectives.

### *Study selection*

Two independent reviewers completed the article study selection (MI, RR). Articles included in the initial search were selected by checking for duplication, title appropriateness, abstract, and inclusion-exclusion criteria. Disputes regarding the paper's eligibility were solved through discussion within the research team.

Data analysis

Data analysis used a data extraction table compiled by a reviewer (MI) and checked by another research team. Information related to study design, participants, interventions, and outcomes were identified. Furthermore, the researchers compiled, summarized, and compared used content analysis. Moreover, the reporting of the study's results used narration form.

RESULTS AND DISCUSSION

The initial search identified 370 articles. The articles were checked for duplication, and 197 articles were eliminated. The selection results based on the title, abstract, and inclusion and exclusion criteria obtained 12 articles. Furthermore, based on identifying the appropriateness of the contents of the full text for review, seven articles met the requirements to be included in the qualitative analysis. The report on the results of the literature selection is illustrated in the PRISMA flow diagram on chart 1, and the data extraction table in table 1.

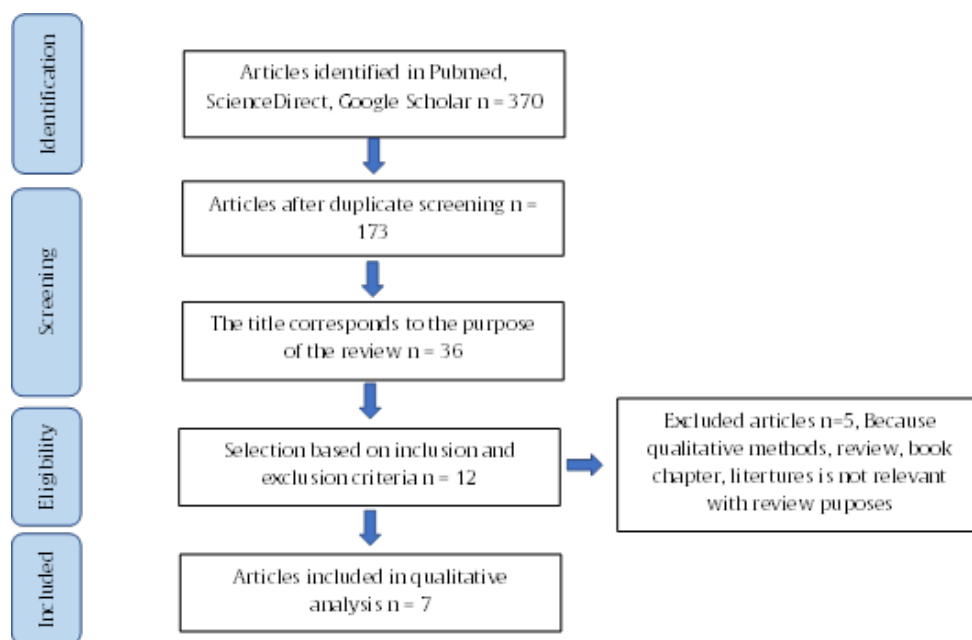


Chart 1. PRISMA flowchart literature selection

Tabel. 1  
 Data Extraction

No	Author, Year publication, Country	Methods	Intervention	Arterial line effectiveness indicators	Results
1	Ishii et al., (2021) Tokyo, Jepang	<b>Method:</b> randomized, controlled, single-blinded clinical trial <b>Sample:</b> Patients in the emergency room and in the Intensive Care Unit with an arterial line installed in the radialis were selected consecutively and randomized into a group receiving normal saline with heparin (n=18) and a group receiving normal saline only (n=16).	The intervention group was given the installation of an arterial line in the radial artery. The normal saline flush was added with heparin in a ratio of 2:1 or two units/cc. Flush developed by pressure bag with 300mmHg pressure to prevent backflow from the artery.	Duration of functioning of the radial arterial line until discharge. The difference in pressure between the arterial line and the pressure in the brachial cuff. Quality of arterial wave pressure	<b>Results</b> Adding heparin to flush fluids has not been shown to increase arterial line patency compared to normal saline alone. Flush without heparin can reduce the risk of HIT (Heparin Induced Thrombocytopenia). <b>Limitation</b> The sample was small, so it is not statistically accurate in detecting minor differences between groups.
2	Tamura et al., (2021) Nagoya, Jepang	<b>Methods:</b> Prospective, triple-blinded, randomized controlled study <b>Sample:</b> 147 ICU	Installation of an arterial line was in the radial artery. In the intervention group, a normal	Incidence of catheter occlusion every 12 hours. Smooth arterial blood sampling every 6	<b>Results</b> There was no difference in the patency of the arterial line for six days between the normal saline-added heparin flushing group and

No	Author, Year publication, Country	Methods	Intervention	Arterial line effectiveness indicators	Results
		surgical patients after surgery with radial arterial lines, were randomly divided into heparin + normal saline (n = 74) and normal saline (n = 73) groups.	saline flush was given with heparin in a ratio of 6:1 or 3000units/500cc NaCl0.9%.	hours. Blood sampling every 24 hours.	the normal saline- group. <b>Limitations</b> Respondents in this study were elective surgery patients who were generally in relatively good condition, so they could not generalize the population with a general condition of severe illness. This study did not identify the side effects of using heparin, such as HIT.
3	Xiong et al., (2019) Nanjing, China	<b>Method:</b> Cohort study <b>Sample:</b> 296 patients (148 in the normal saline group and 148 in the heparin group) who had a similar risk profile and underwent cardiac surgery.	Installation of an arterial line in the radial artery with normal saline flush compared with normal saline flush with heparin.	The patency of the cannula was measured whether the catheter is smooth or not when taking blood. Reliability of arterial pressure by comparing line arterial pressure with brachial cuff blood pressure measurements. Called reliable if the pressure difference is approximately 10 mmHg. Good arterial waveform.	Based on the study's results, adding heparin to normal saline as a flush for arterial pressure monitoring did not reduce the incidence of thrombosis/clotting in the catheter. The addition of heparin only had a significant effect on increasing ACT and APTT.
4	Alizadehasl (2015) Iran	<b>Method:</b> Double-blind randomized clinical trial. <b>Sample:</b> 100 patients who underwent elective cardiac surgery. Patients were randomized into two groups, namely the group with normal saline plus heparin (n=50) and the normal saline group without heparin (n=50).	Installation of an arterial line in the radial artery. In the intervention group, normal saline flush was given with heparin in a ratio of 10:1 or 10unit/cc.	Arterial pressure waveforms were measured on the first, second, and third days.	<b>Results:</b> This study showed that the arterial pressure waveforms in the heparin group and the normal saline group on the first, second and third days were not statistically different. Use of normal saline as an alternative to normal saline given heparin may be a safer solution in the short term in post-cardiac surgery patients. <b>Limitations:</b> The patient population is limited to cardiac surgery patients so that it cannot generalize to other patient populations. The number of samples is limited to 100 samples. The duration of monitoring is only 3 days because the average cardiac surgery patient uses an arterial line for 3 days.
5	Ziyaeifard et al., (2015) Tehran, Iran	<b>Method:</b> Double-blind randomized clinical trial. <b>Sample:</b> 100 patients who underwent coronary and heart valve surgery. Patients were randomized into two groups, namely the group with normal saline plus heparin (n=50) and the normal saline group without heparin (n=50).	Installation of an arterial line in the radial artery and a central venous catheter in the subclavian vein. In the intervention group, normal saline flush was given with heparin in a ratio of 10:1 or 5000 units/500ml physiological NaCl.	The patency of the arterial line or central venous catheter was measured for 3 days after cardiac surgery.	<b>Results:</b> Based on the results of the study the use of heparin in normal saline did not prolong the duration of patent arterial line and central venous catheter. Normal saline can be used as the standard fluid to prevent catheter occlusion after cardiac surgery. Normal use of saline without heparin can prevent heparin-induced complications such as allergic reactions, local tissue damage, bleeding, and heparin-induced thrombocytopenia. <b>Limitations:</b> Patency duration was only measured for 3 days postoperatively and could not measure long term.

No	Author, Year publication, Country	Methods	Intervention	Arterial line effectiveness indicators	Results
6	Han et al., (2012) Seoul, Korea Selatan	<b>Methods:</b> Nonequivalent control group, non-synchronized, double-blind experimental study. <b>Sample:</b> 109 patients who underwent surgery and required hemodynamic monitoring of arterial pressure during surgery. Patients were randomly assigned to a normal saline group (n=59) and a normal saline group with heparin (n=55).	Installation of an arterial line in the radial artery. In the intervention group, normal saline flush was given with heparin in a ratio of 2:1 or 2unit/cc.	<ul style="list-style-type: none"> <li>Patent arterial line during operation.</li> <li>Coagulation values.</li> </ul>	<b>Results:</b> There was no difference in duration of patent during surgery between the heparin group and the normal saline group. There was no difference in APTT values between the heparin group and the normal saline group.
7	Goh et al., (2011) Singapura	<b>Methods:</b> Single-blind Randomized Controlled Trial. <b>Sample:</b> 70 patients who were admitted to Neuro Science ICU and needed monitoring of arterial pressure and central venous pressure. Patients were randomly assigned to a normal saline group (n=36) and a normal saline group with heparin (n=34).	Installation of artery catheters in the radial and central veins with a triple lumen catheter. Which is connected to the transducer with a pressure bag with a pressure of 300mmHg. In the normal saline group with heparin, the dose of heparin added to 500cc of 0.9% NaCl was 500 units (1:1).	The functioning of the arterial line and the cv catheter as determined by the waveform and the presence or absence of blood backflow were monitored at 72 hours and 120 hours after insertion.	<b>Results:</b> The study found no significant difference between the 2 fluids used to maintain the patency of the central venous and arterial catheters. Reducing the use of heparin in flush fluids will reduce the potential for adverse events and reduce costs. <b>Limitations:</b> This study was only conducted in NSICU and cannot generalize to the population. Monitoring the duration of use of AL and CVL also uses time intervals instead of actual hours so that it cannot calculate the average duration of use of AL and CVL.

### Study characteristics

Of the seven articles reviewed, six were Randomized Controlled Trials (RCT), and one article was a cohort study. All studies from Asia consisted of two studies from Japan, two from Iran, and one study each from China, Korea, and Singapore. The total participants were 856 patients and were treated in surgical/medical ICU or Emergency Unit. Most of the participants were post-cardiac surgery patients (n=496). Most arterial line installations were in the radial artery, and a small proportion was placed on the femoral or dorsalis pedis arteries.

In the group that was given flushing heparin with normal saline, the interventions carried out in each study were different, especially regarding the ratio of heparin and normal saline doses, which was 1:1 (Goh et al., 2011; Xiong et al., 2019) 2:1 (Han et al., 2012; Ishii et al., 2021), 6:1 (Tamura et al., 2021), and 10:1 (Alizadehasl et al., 2015; Ziyaeifard et al., 2015). In terms of research outcomes, five articles discussed the duration of arterial line patency. The duration of the patent was determined by the time from the patient was inserted until it was removed because the arterial line was no longer needed or there was a blockage (clotting) of the catheter (Alizadehasl et al., 2015; Han et al., 2012; Ishii et al., 2021; Tamura et al., 2021; Xiong et al., 2019). In addition, three articles discuss the quality of the

arterial waves generated by transducers on monitors. Two articles discuss comparing arterial pressure with brachial cuff measurement pressures, which is reliable when the difference is not more than 10mmHg. The study of Han et al. (2012) was the only article discussing differences in blood coagulation values through APTT measurements.

Heparin has often been used as a flushing fluid to maintain arterial line patency, but the use of heparin is still controversial. The basis for consideration of this view is that heparin is not a thrombolytic agent that can destroy blockages but prevents the occurrence of blockages by inhibiting factors associated with the process of formation of blockages. In addition, there was no valid research evidence regarding the composition of heparin and its appropriate dilution and producing a therapeutic effect on the arterial line while at the same time not causing undesirable side effects (Bertoglio et al., 2012).

An essential thing in the effectiveness of the arterial line is the long duration of functioning and avoiding the formation of blockages. This condition will determine clinical decisions and reduce the risk of arterial line re-insertion that could harm the patient due to repeated invasive procedures (Lee & Della, 2014). Based on the results of the review, it was identified that there was no difference in the use of heparin flushing compared to normal saline in arterial line patency or obstruction (Alizadehasl et al., 2015; Han et al., 2012; Ishii et al., 2021; Tamura et al., 2021; Xiong et al., 2019), even

with the highest dose with a ratio of heparin and normal saline 10:1 (Alizadehasl et al., 2015).

The patency of the arterial line also determines the accuracy of the arterial wave (dampening), which can be a sign of the effectiveness of the arterial line. Three studies discussed arterial line patency with this arterial wave (Alizadehasl et al., 2015; Ishii et al., 2021; Xiong et al., 2019). The three studies showed no significant difference in arterial waves in the two groups. The rate of arterial patency and the better waveform in normal saline without heparin could be since arterial line device settings are improving. Likewise, arterial line treatment protocols are increasingly developing (Ishii et al., 2021). The results of these studies also stated that the patency of the catheter was not determined by the presence or absence of an anticoagulation agent but was determined by the constant flushing of the fluid (Goh et al., 2011).

The results of this study indicate that the longest duration of arterial line placement that can be measured was five days (120 hours), so it has not been able to prove the effectiveness of normal saline in maintaining arterial line patency in the longer term (Tully et al., 2014). A systematic review study by Kordzadeh et al. (2014) stated that using heparin as a flush is better in long-term arterial line usage. Therefore, in patients who require long-term use of an arterial line, heparin as a flushing method may be recommended while monitoring side effects such as Heparin-Induced Thrombocytopenia (HIT), hematoma, and bleeding (Bertoglio et al., 2012).

## LIMITATION OF THE STUDY

The lack of databases in literature searching, language restrictions, and also year of publication limitation might allow similar articles from other sources failed to be identified. In addition, These weaknesses can lead to a lack of exploration of the results of publications on related topics.

## CONCLUSIONS AND SUGGESTIONS

There was no significant difference in the effectiveness of the patency arterial line between the use of normal saline flushing with heparin with normal saline. The use of normal saline without adding heparin as a flush is recommended particularly for shorter time because it reduces the risk of Heparin-Induced Thrombocytopenia (HIT), allergy to heparin, and bleeding and is economically more cost-saving. It is necessary to investigate the difference in the effectiveness of the patency arterial line with a longer arterial line (more than five days).

## Conflict of Interest Statement

The Authors declare that there is no conflict of interest.

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