

# Analysis of the Integrated Management Model of Medical Care and Medication in Intravenous Treatment for Critically Ill Patients

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**Objective:** To explore the effect of the Integrated Management Model of Doctor-Nurse-Pharmacist Collaboration on the Safety of Intravenous Therapy in Critically Ill Patients.

**Methods:** 1587 patients who were hospitalized in the Intensive Care Department of the Fourth Hospital of Hebei Medical University in China from January 2021 to December 2022 were selected. 768 patients before the implementation of the integrated medical, nursing, and drug management model were selected as the control group, and 819 patients who implemented the integrated medical, nursing, and drug management model were selected as the observation group.

**Results:** Compared with the control group, the incidence of drug compatibility contraindications in the observation group decreased from 3.5% to 1.5% ( $\chi^2=6.957$   $P=0.008$ ), the central venous catheter (CVC) blockage rate decreased from 2.5% to 1.0% ( $\chi^2=5.249$   $P=0.022$ ), the daily incidence of catheter related bloodstream infections decreased from  $(1.84 \pm 2.17)$  to  $(0.91 \pm 1.19)$  ( $t=6.988$   $P=0.015$ ), and the incidence of peripheral venous treatment related complications decreased from 10.3% to 2.9% ( $\chi^2=16.663$   $P=0.000$ ). Among them, the incidence of phlebitis decreased from 5% to 1.6% ( $\chi^2=4.817$   $P=0.028$ ). The incidence of drug exudation decreased from 3.4% to 0.8% ( $\chi^2=0.031$   $P=0.019$ ). The incidence of extravasation has decreased from 2.5% to 0.4% ( $\chi^2=0.044$   $P=0.027$ ). The differences were statistically significant ( $P<0.05$ ).

**Conclusion:** The Integrated Management Model of Doctor-Nurse-Pharmacist Collaboration significantly reduced the incidence of catheter-related bloodstream infections (CRBSI), drug incompatibility, and other intravenous therapy-related complications, thereby enhancing the safety of intravenous therapy in critically ill patients.

**Keywords:** severe patients, integration of doctor-nurse-pharmacist, intravenous treatment safety, complication

## Introduction

According to a report from the National Medical Products Administration in 2020,<sup>1</sup> adverse drug reactions/events caused by injectable medication in China accounted for 56.7%, among which 91.1% were attributed to intravenous administration. Reliable intravenous infusion routes are crucial means for rescuing and treating critically ill patients in the intensive care unit (ICU). Critically ill patients in the ICU require a wide range of medications, with diverse types and significant variability, and thus are at higher risk of developing adverse reactions. Studies in South America indicate that drug incompatibility is more prevalent in the ICU than in general wards.<sup>2</sup>

Considering the high severity of their conditions, the complexity of treatment regimens, and the necessity for combined and diverse therapies, ICU patients often require simultaneous administration of multiple intravenous infusions, posing significant risks and challenges to intravenous injection (IVT) safety.<sup>3</sup> It is difficult to ensure medication and IVT safety for critically ill patients through the sole participation of nursing professionals.<sup>4</sup> Surveys have shown that nurses have a relatively low level of awareness regarding intravenous drug incompatibility, with limited sources of knowledge, and significant cognitive differences among nurses at different levels.<sup>5</sup> The observed rise in catheter-related

complications in critically ill patients despite the availability of established guidelines. These complications not only increase patient morbidity but also extend ICU stays and healthcare costs.<sup>6–8</sup> Although previous studies have examined interventions such as improved catheter maintenance and infection control protocols, these efforts primarily focus on isolated aspects of care, with limited research exploring a more integrated approach.<sup>9,10</sup>

Integrated medical care is a patient-centered, integrated treatment and nursing model formed through close coordination between doctors, pharmacists and nursing staff. This model can fully leverage the collaborative leadership and active participation of doctors and nursing staff, strengthen multidisciplinary collaboration, and enhance the quality of therapeutic nursing care.<sup>11</sup> Studies have also demonstrated that the involvement of clinical pharmacists can enhance medication safety management and effectively prevent adverse drug events, playing a crucial role in ensuring medication safety during hospitalization.<sup>12</sup> This model provides comprehensive management of ICU patients, leading to improved clinical outcomes, reduced incidence of complications in ICU patients, increased patient survival rates, and provision of individualized, continuous treatment and nursing care, meeting the psychological and social needs of patients and their families.<sup>13</sup> Surveys have shown that there are numerous issues with the use and management of central vascular access devices in secondary and tertiary hospitals in Hebei Province, with a high risk of complications.<sup>14</sup> In recent years, various associations and organizations worldwide have successively released and updated guidelines and expert consensus on intravenous infusion therapy.<sup>15</sup>

This study is designed to address a gap in existing practices and guidelines—specifically, the lack of a coordinated, multidisciplinary approach to intravenous therapy management in critically ill patients. By implementing a Doctor-Nurse-Pharmacist Integrated Management Model, we hypothesize that a collaborative strategy will lead to a more significant reduction in intravenous therapy complications than existing methods. The primary objective of this study is to evaluate the effect of the integrated management model on the safety of intravenous therapy in critically ill patients, focusing on outcomes such as the incidence of CRBSI, drug incompatibility, CVC occlusion, and other therapy-related complications. By examining the effectiveness of this multidisciplinary approach, we aim to provide new insights into improving patient outcomes in the ICU setting.

## Materials and Methods

### Study Design

This is a retrospective, comparative study conducted on critically ill patients admitted to the ICU of the Fourth Hospital of Hebei Medical University from January 2021 to December 2022.

### Subject Recruitment and Sample Size

A total of 1587 critically ill patients were included in the study, with 768 patients in the control group and 819 patients in the observation group. Subjects were recruited based on the following inclusion and exclusion criteria. A post-hoc power analysis was conducted to confirm that the sample size was adequate to detect statistically significant differences between the groups. The study achieved a power of 80%, ensuring that the sample size is sufficient to observe meaningful outcomes in terms of reduced complication rates.

The inclusion criteria are as follows: (1) history of the central venous catheter (CVC) or peripherally inserted central catheter (PICC) placement, (2) concurrent use of two or more infusions, and (3) provision of signed informed consent. The exclusion criteria are as follows: (1) CVC or PICC dwell time less than 48 hours, or (2) presence of catheter-related bloodstream infection (CRBSI) at the time of admission.

**Rationale for Including Patients with CVC, PICC, and Peripheral Catheters:** The enrolled patients in the study included those with CVCs, PICCs, and peripheral venous catheters to provide a comprehensive evaluation of intravenous therapy safety in the ICU setting. Critically ill patients often require multiple types of intravenous access throughout their treatment, depending on their clinical needs and the duration of their hospital stay. Evaluating all types of catheter-related complications allows for a holistic assessment of intravenous therapy safety and ensures that the study findings are applicable across the full spectrum of clinical practice.

## Group Allocation

The control group comprised patients who received standard intravenous therapy care prior to the implementation of the integrated management model. The observation group included patients who were treated after the integrated Doctor-Nurse-Pharmacist management model was introduced. No randomization was used, as this was a retrospective analysis based on historical patient data.

## Methods

### Team Composition and Involvement

The IVT team consisted of 20 members in total, including 2 specialists, 1 pharmacist, 3 head nurses, and 9 IVT specialty nurses. Different responsibilities were allocated to the team members. The head nurse of the department was appointed as the team leader, responsible for overall management tasks such as communication, coordination, and organization. The deputy head nurses were assigned to draft and revise IVT-related departmental protocols, operational standards, training plans, and adverse event reporting procedures, as well as oversee their implementation. Both specialists, holding the title of chief physicians, were responsible for formulating medication regimens for critically ill patients and providing guidance for the development of IVT-related departmental protocols. The pharmacist was responsible for adjusting medication regimens, providing guidance and training on medication safety, and participating in the development of IVT-related departmental protocols. The IVT specialty nurses were responsible for training on IVT-related departmental protocols and knowledge, as well as conducting IVT quality control checks.

These team members were responsible for the overall management of intravenous therapy. While the entire team developed protocols and provided training, typically 4–6 team members were directly involved in the therapy application and monitoring for each patient, depending on the complexity of the patient's condition and the required level of care.

### Development of the “Choice of Intravenous Therapy Access for Patients in Intensive Care Unit and Maintenance Management System” and the “Common Drug Incompatibility List for Patients in Intensive Care Unit” (Hereinafter Referred to as the Management System and the Drug Incompatibility List, Respectively)

The Management System includes four sections: indications for placement of commonly used vascular access devices in ICU, choice of IVT infusion routes, replacement of infusion devices and accessories, and maintenance of vascular access. The Drug Incompatibility List was compiled by the pharmacist after retrieving 20 commonly used drugs in the ICU from the Micromedex rational drug use system.<sup>16</sup> This list describes the compatibility of each pair of drugs at four levels: incompatible, not recommended, uncertain, and recommended, providing clinical nurses with valuable references for IVT. Both the Management System and the Drug Incompatibility List were drafted based on evidence-based practice and revised through multiple discussions in specialist-nurse-pharmacist meetings.

### Implementation of Specialist-Nurse-Pharmacist Morning Rounds

During morning rounds, the attending physician and the responsible nurse provide reports on the patient's condition from medical and nursing perspectives, respectively. The pharmacist proposes medication adjustment plans and medication precautions based on the previous day's administration and laboratory test results. After physical examinations, the responsible chief physician comprehensively analyzes the patient's condition under the guidance of the specialist-nurse-pharmacist team, formulating a treatment regimen and specific objectives for the day. During ward rounds, doctors and nurses jointly assess the necessity of retaining catheters, especially CVC placement and removal. Following rounds, the responsible nurse devises a nursing care plan and measures of the day based on the corresponding treatment plan and objectives.

### Implementation of Regular IVT Training and Quality Control

The department conducts quarterly training and assessments on the Management System and IVT-related knowledge for all nursing staff. The Management System is incorporated into the regular training course designed for newly recruited nurses, including interns, specialist nurses, and newly hired nurses. Quality control standards for IVT are established, with weekly controls and monthly comprehensive analysis and improvement. In the event of adverse events, responsible nurses must report them via the hospital's adverse events and safety management system during their shift.

## Assessed Parameters and Outcome Evaluation

We measured medication safety by tracking the incidence of the following indicators, which were chosen as the primary outcomes, and the evaluation was based on established guidelines such as the “Guidelines for the Prevention and Control of Vessel Catheter-Associated Infection (2021 Edition)”.<sup>17</sup>

(1) Incidence of drug incompatibility: When dispensing medication, nurses or the pharmacist should observe the drug incompatibility rate. It is essential to choose the appropriate catheter type based on the drug’s characteristics.

The incidence of drug incompatibility was defined as any *in vitro* interaction that occurs after the mixing of two drugs, resulting in abnormal appearances such as turbidity, precipitation, gas generation, or discoloration. This outcome was measured by the pharmacist through regular checks and recorded if any drug compatibility issues were observed. Certain drugs require a catheter with a central tip due to their chemical properties and the risk of causing irritation or incompatibility when administered peripherally. Manrique-Rodríguez et al discuss the standardization of intravenous therapy in adult patients, highlighting the necessity of using catheters with central tips for specific drug types to prevent complications like phlebitis or drug incompatibility.<sup>18</sup> Similarly, Borgonovo et al provide practical recommendations for intravenous antimicrobial administration, emphasizing the use of catheters with central tips for drugs with known irritant properties to ensure safe and effective therapy.<sup>19</sup>

(2) Complications related to peripheral intravenous therapy (PIVT), such as venitis, drug extravasation, and drug infiltration: After peripheral venous catheterization, nurses should be vigilant about complications related to peripheral intravenous therapy (PIVT), especially the incidence rates of venitis, drug extravasation, and drug infiltration. Evaluation criteria refer to the Infusion Therapy Standards of Practice (8th Edition) published by the American Nursing Association in 2021.<sup>17</sup> These were defined as follows:

Phlebitis: Inflammation of a vein associated with pain, redness, or swelling at the site of catheter insertion, evaluated based on the Infusion Therapy Standards of Practice (8th Edition).<sup>17</sup>

Drug Infiltration: The leakage of medication from the vein into surrounding tissues, noted by the presence of swelling, pain, or skin discoloration.

Drug Extravasation: The inadvertent administration of vesicant or irritant medications into surrounding tissue, confirmed by visible tissue damage or ulceration.

(3) Incidence of CVC occlusion and CRBSI: After PICC placement, nurses should pay attention to CVC-related complications during routine observation, especially the incidence rates of CVC occlusion and CRBSI. The diagnostic criteria for CRBSI refer to the Guidelines for the Prevention and Control of Vessel Catheter-Associated Infection (2021 Edition) released by the National Health Commission.<sup>17</sup>

The incidence of CVC occlusion was defined as the occurrence of any obstruction in the catheter lumen that impedes or prevents the administration of fluids or medication. This was identified and recorded by nursing staff during routine catheter maintenance or medication administration.

The daily incidence of CRBSI was calculated as the number of infections per 1000 catheter days, diagnosed based on clinical symptoms (fever, chills) and confirmed by positive blood culture results. The diagnostic criteria followed the “Guidelines for the Prevention and Control of Vessel Catheter-Associated Infection (2021 Edition)”.<sup>17</sup>

## Statistical Analysis

All statistical analyses were performed using SPSS version 20.0. Normally distributed measurement data were presented as “mean  $\pm$  standard deviation ( $\bar{x} \pm s$ )”, and comparisons within groups were examined using independent sample *t*-tests. Rates were expressed as percentages (%), and comparisons within groups were analyzed using chi-square tests. Unless otherwise specified,  $P < 0.05$  indicates a difference of statistical significance. Thank you for your constructive feedback. Based on your suggestions, we have carefully reviewed the methods and results sections and made the necessary revisions to ensure clarity and completeness. Specifically, we have updated the notes in the tables to include the full definitions of abbreviations to improve the readability and understanding of the data.

## Results

### General Patient Data of the Control and Observation Groups

There were no significant differences in gender, age, Acute Physiology and Chronic Health Evaluation (APACHE-II) scores, and ICU average length of stay between the two groups (all  $P > 0.05$ ). See [Table 1](#).

### Comparison of Drug Incompatibility Rates Between the Control and Observation Groups

The comparison of drug incompatibility rates between the control and observation groups was conducted using the  $\chi^2$ -test. The results showed that compared with the control group, the drug incompatibility rate in the observation group decreased from 3.5% to 1.5% ( $\chi^2 = 6.957$ ,  $P = 0.008$ ), suggesting a statistically significant difference between the two groups ( $P < 0.05$ ). See [Table 2](#).

### Comparison of CVC-Related Complications Between the Control and Observation Groups

The incidence rates of CVC-related complications in the two groups were compared, and the results showed that compared with the control group, the CVC occlusion rate in the observation group decreased from 2.5% to 1.0% ( $\chi^2 = 5.249$ ,  $P = 0.022$ ), and the occurrences of CRBSI per 1000 catheter days decreased from (1.84±2.17) to (0.91±1.19) cases ( $t = 6.988$ ,  $P = 0.015$ ). The differences were statistically significant ( $P < 0.05$ , respectively). See [Table 3](#).

**Table 1** General Patient Data Between the Control and Observation Groups

Parameter	Control group (n = 768)	Observation group (n = 819)	$\chi^2/t$	P
Sex (n, %)				
Male	474(61.7%)	479(58.5%)	1.727	0.189
Female	294(38.3%)	340(41.5%)		
Age	63.34±14.47	64.32±12.17	0.748	0.118
APACHEII	15.27±8.46	16.48±9.89	1.448	0.224
ICU LoS	8.55±7.27	9.59±7.82	1.447	0.210

**Note:** Data were presented as "mean ± standard deviation ( $\bar{x} \pm s$ )".

**Abbreviations:** APACHE-II, acute physiology and chronic health evaluation; ICU, intensive care unit.

**Table 2** Comparison of Incidence of Incompatibility Between the Control and Observation Groups

Incompatibility	Control group (n, %)	Observation group (n, %)	$\chi^2$	P
Present	27(3.5%)	12(1.5%)	6.957	0.008
Absent	741(96.5%)	807(98.5%)		

**Table 3** Comparison of Venous Catheter-Related Complications Between the Control and Observation Groups

Parameter	Control group (n, %)	Observation group (n, %)	$\chi^2/t$	P
CVC occlusion				
Present	19(2.5%)	8(1.0%)	5.249	0.022
Absent	749(97.5%)	811(99.0%)		
CRBSI incidence rate per 1000 catheter days (frequency)	1.84±2.17	0.91±1.19	6.988	0.015

**Note:** Data were presented as "mean ± standard deviation ( $\bar{x} \pm s$ )".

**Abbreviations:** CVC, central venous catheter; CRBSI, catheter-related bloodstream infection.

**Table 4** Comparison of Peripheral Intravenous Therapy-Related Complications Between the Control and Observation Groups

Parameter	Control group	Observation group	$\chi^2$	P
PVC (n, %)				
Used	203(26.4%)	488(59.6%)	177.203	0.000
Not used	565(73.6%)	331(40.4%)		
Overall related complication rate (n, %)				
Present	79(10.3%)	24(2.9%)	16.663	0.000
Absent	689(89.7%)	795(97.1%)		
Venitis (n, %)				
Present	38(4.9%)	13(1.6%)	4.817	0.028
Absent	730(95.1%)	806(98.4%)		
Drug infiltration (n, %)				
Present	26(3.4%)	7(0.8%)	0.031	0.019
Absent	742(96.6%)	812(99.2%)		
Drug extravasation (n, %)				
Present	19(2.5%)	3(0.4%)	0.044	0.027
Absent	749(97.5%)	816(99.6%)		

**Abbreviation:** PVC, premature ventricular contraction.

Comparison of PIVT-Related Complications Between the Control and Observation Groups

The PVC utilization rates in the two groups were compared, and the results showed that compared with the control group, the PVC utilization rate in the observation group increased from 26.4% to 59.6%, and the difference was statistically significant ( $P < 0.05$ ). See Table 4.

The overall PIVT-related complication rates in the two groups were compared, and the results showed that compared with the control group, the overall PIVT-related complication rate in the observation group decreased from 10.3% to 2.9%, and the difference was statistically significant ( $P < 0.05$ ). Specifically, the incidence of phlebitis significantly decreased from 4.9% to 1.6% ( $P < 0.05$ ); the incidence of drug extravasation significantly decreased from 3.4% to 0.8% ( $P < 0.05$ ); the incidence of drug infiltration significantly decreased from 2.5% to 0.4% ( $P < 0.05$ ). See Table 4.

Discussion

The implementation of the integrated management model of doctor-nurse-pharmacist collaboration demonstrated a significant impact on reducing intravenous therapy-related complications in critically ill patients. Specifically, the incidences of CRBSI and CVC occlusion significantly decreased in the observation group compared to the control group, as evidenced by the reduced daily CRBSI incidence from  $(1.84 \pm 2.17)$  per 1000 catheter days in the control group to  $(0.91 \pm 1.19)$  in the observation group ( $P = 0.015$ ), and the reduction in CVC occlusion from 2.5% to 1.0% ( $P = 0.022$ ). These results underscore the effectiveness of multidisciplinary collaboration in enhancing the safety of intravenous therapy.

In this study, pharmacists developed the Drug Incompatibility List based on evidence-based practice. This list provides clear compatibility recommendations for each pair of the 20 commonly used drugs in the ICU, offering scientific, clinically beneficial guidance for nurses. The Management System, jointly established by doctors, nurses, and a pharmacist, provides explicit guidelines for the choice of infusion routes. The integration of a pharmacist into the care team played a crucial role in reducing drug incompatibilities, which fell from 3.5% to 1.5% in the observation group ( $P = 0.008$ ). This highlights the value of incorporating pharmacists into the management of critically ill patients to mitigate medication-related risks.

The integrated management model<sup>20</sup> is formed by a relatively stable medical team consisting of specialists, a licensed pharmacist, and professional nurses, breaking through the previous limitations of nurses solely undertaking IVT. Within



the integrated management framework, specialists, nurses, and a pharmacist jointly formulate departmental protocols and attend ward rounds, playing complementary, advisory, supervisory, and executive roles in the team to devise the best treatment plans for patients. This model facilitates communication and collaboration among the three parties and ensures IVT quality control and assurance. The study by Ying L<sup>21</sup> reported a significant decrease in the overall incidence of hospital-acquired infections in the ICU through specialist-nurse integrated infection control management for critically ill patients. The studies by Menegueti MG,<sup>22</sup> Carmel,<sup>23</sup> and Agnihotri V<sup>24</sup> et al showed that the doctor-nurse collaborating model can reduce the incidence of CVC-related infections and PICC-related complications. This finding has been confirmed by Lv Y et al<sup>25</sup> and Wang Shan et al.<sup>26</sup> Our findings align with these previous studies that explored interventions such as doctor-nurse collaboration in reducing hospital-acquired infections and improving patient outcomes.<sup>6,9,20,21</sup> However, our study distinguishes itself by integrating a pharmacist into the care team, which has shown to be a key factor in further reducing the incidence of drug incompatibility (from 3.5% to 1.5%) and other complications. This setting can improve targeted, rational drug use, reducing adverse drug reactions and the incidence of IVT-related complications. This difference highlights the additional value that a pharmacist brings to the integrated management model, especially in complex ICU environments where drug interactions and catheter-related complications are prevalent. Following the implementation of the integrated management model in this study, the utilization rate of peripheral intravenous indwelling needles significantly increased from 26.4% in 2021 to 59.6% in 2022, while the incidence rate of PIVT-related complications significantly decreased in 2022 compared with the previous year ( $P < 0.05$ , respectively). In 2022, the occurrences of CRBSI per 1000 catheter days decreased from  $(1.84 \pm 2.17)$  cases in 2021 to  $(0.91 \pm 1.19)$  cases, and the incidence rate of CVC occlusion decreased from 2.5% to 1.0%, demonstrating statistically significant differences ( $P < 0.05$ , respectively), further supporting the benefits of the integrated management model.

In critically ill cases, IVT involves the selection, establishment, and maintenance of vascular access, as well as the administration of various drugs, including combinations of special drugs and fluid management. This entails a high risk of IVT-related complications in critically ill patients, necessitating an integrated approach to achieve evidence-based management. The establishment of an integrated IVT team and the development of protocols are fundamental to management in this study. The core of management lies in mobilizing doctors, nurses, and a pharmacist for morning rounds, while regular team training and quality control serve as robust guarantees for the standardization and homogenization of management practice. The integrated management model enhances communication and collaboration among doctors, nurses, and pharmacists, reducing the incidence of IVT-related complications and ensuring medication and IVT safety for critically ill patients. However, there are limitations in the selection of study subjects and the standardization of protocol development. Constructing a scientifically sound integrated management plan and strengthening IVT safety management for critically ill patients remain key concerns for critical care healthcare professionals in the future.

This study has some limitations. (1) This study only selected ICU patients from one hospital as the study subjects, lacking multicenter data support, which may limit the universality and generalizability of the study results. (2) This study adopted a retrospective design with before-and-after comparisons, which carries potential biases inherent in retrospective designs and makes it difficult to exclude the influence of other interventions or external factors on the results. Some external factors that could have contributed to the observed improvements include advancements in general ICU protocols, such as updated infection control practices or catheter care guidelines, which may have been implemented during the study period. Additionally, as ICU staff gained more experience and training in intravenous therapy over time, this could have independently improved patient outcomes. Finally, differences in the patient population characteristics, such as the severity of illness or demographic changes, could have affected the complication rates and must be considered when interpreting the results. (3) While this study included a sample size of 1587 patients, which provides adequate statistical power for detecting differences in complication rates, there are limitations that may affect the generalizability of the findings. The study was conducted in a single institution over a specific time period, which may introduce selection bias. The results, therefore, may not fully reflect the broader population of critically ill patients in other settings. (4) Some observation indicators, such as drug incompatibility and complication rates, were only analyzed as quantitative parameters, lacking qualitative observations of the specific conditions and clinical manifestations of patients. (5) While our primary objective was to evaluate the overall safety of intravenous therapy in critically ill patients

using an integrated management model, the specific number of lumens for each CVC was not systematically recorded. This may affect the interpretation of our findings regarding CRBSI, occlusions, and other CVC-related complications, as the number of lumens is known to influence these outcomes. (6) The interpretation of the results in this study is relatively simple, without delving into the potential problems, obstacles, and corresponding improvement methods related to the implementation of the integrated management model. (7) This study has its limitations in the selection of study subjects and the standardization of departmental protocols, warranting further discussion and resolution regarding their impact on the study results.

## Conclusion

The Doctor-Nurse-Pharmacist Integrated Management Model can significantly reduce the occurrence of IVT-related complications in critically ill patients, including drug incompatibility, CVC occlusion, CRBSI, and PIVT-related complications. This collaborative approach can effectively ensure IVT safety for critically ill patients and offers a promising strategy for improving intravenous therapy safety in critically ill patients, and it should be further explored and refined in future studies.

## Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

## Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Fourth Hospital of Hebei Medical University.

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## Disclosure

All of the authors had no any personal, financial, commercial, or academic conflicts of interest separately.

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