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Original Article

Prevention of urinary tract infection using a silver alloy hydrogel-coated catheter in critically ill patients: A single-center prospective randomized controlled study

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ABSTRACT

Background: A new type of silver alloy hydrogel-coated (SAH) catheter has been shown to prevent bacterial adhesion and colonization by generating a microcurrent, and to block the retrograde infection pathway. However, these have only been confirmed in ordinary patients. This study aims to evaluate the effectiveness of a SAH catheter for preventing urinary tract infections in critically ill patients.

Methods: This was a prospective single-center, single-blind, randomized, controlled study. A total of 132 patients requiring indwelling catheterization in the intensive care unit (ICU) of the First Affiliated Hospital of the University of Science and Technology of China between October 2022 and February 2023 and who met the study inclusion/exclusion criteria were randomly divided into two groups. Patients in the SAH catheter group received a SAH catheter, while patients in the conventional catheter group received a conventional siliconized latex Foley catheter. The main outcome measure was the incidence of catheter-associated urinary tract infections (CAUTIs). Secondary outcome indicators included urine positivity for white blood cells and positive urine cultures on 3 days, 7 days, 10 days, and 14 days after catheterization, number of viable bacteria in the catheter biofilm on day 14, pathogenic characteristics of positive urine cultures, length of ICU stay, overall hospital stay, ICU mortality, and 28-day mortality. All the data were compared between the two groups.

Results: A total of 68 patients in the conventional catheter group and 64 patients in the SAH catheter group were included in the study. On day 7 after catheter placement, the positivity rate for urinary white blood cells was significantly higher in the conventional catheter group than in the SAH catheter group (33.8% *vs.* 15.6%, P=0.016). On day 10, the rates of positive urine cultures (27.9% *vs.* 10.9%, P=0.014) and CAUTIs (22.1% *vs.* 7.8%, P=0.023) were significantly higher in the conventional catheter group than in the SAH catheter group. On day 14, the numbers of viable bacteria isolated from the catheter tip ($[3.21\pm1.91]\times10^6$ colony-forming units [cfu]/mL *vs.* $[7.44\pm2.22]\times10^4$ cfu/mL, P <0.001), balloon segment ($[7.30\pm1.99]\times10^7$ cfu/mL *vs.* $[3.48\pm2.38]\times10^5$ cfu/mL, P <0.001), and tail section ($[6.41\pm2.07]\times10^5$ cfu/mL *vs.* $[8.50\pm1.46]\times10^3$ cfu/mL, P <0.001) were significantly higher in the conventional catheter group than in the SAH catheter group. The most common bacteria in the urine of patients in both groups were *Escherichia coli* (n=13) and *Pseudomonas aeruginosa* (n=6), with only one case of *Candida* in each group. There were no significant differences between the two groups in terms of ICU hospitalization time, total hospitalization time, ICU mortality, and 28-day mortality.

Conclusion: SAH catheters can effectively inhibit the formation of catheter-related bacterial biofilms in critically ill patients and reduce the incidence of CAUTIs, compared with conventional siliconized latex Foley catheters; however, regular replacement of the catheter is still necessary.

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Introduction

Catheter-associated urinary tract infections (CAUTIs) are among the most commonly reported hospital-acquired infections. Jacobsen et al.[1] reported that more than 1 million patients in the United States suffer from CAUTIs every year, accounting for 40% of all hospital-acquired infections, next to respiratory system infections, while the proportion of CAUTIs in China is also as high as 15–34%.[2] About 20% of cases of hospital-acquired bacteremia are due to CAUTIs, associated with an increase in mortality of hospitalized patients of about 10%.[3] The intensive care unit (ICU) is heavily impacted by CAUTIs; although many patients receive prophylactic or therapeutic antibiotics, CAUTIs are still difficult to resist. This may be closely related to the formation of bacterial biofilms on the surface of the catheter. Longer catheter retention times allow the biofilm on the catheter surface to become more solid, leading to possible blockage, and also forming a source of infections.[4] In addition, bacteria or fungi in the biofilm can be resistant to antibiotics independently of drug-resistance genes, forming a protective membrane-like structure through a self-produced polysaccharide matrix and fibrin complex.[5]

Evidence suggests that strict aseptic procedures during indwelling catheter placement and shortening the duration of catheterization can significantly reduce the incidence of CAUTIs in the hospital.[6] In addition, biofilm formation can be prevented by changing the material of the catheter surface to reduce the incidence of CAUTIs, and various coated urinary catheters have demonstrated advantages compared with traditional silicone and latex catheters that have been applied in clinical settings. For example, silver-coated and nitrofural-coated catheters have been used clinically since the early 2000s; however, although they can reduce the incidence of CAUTIs,[7] they also have certain side effects, such as patient discomfort associated with nitrofural-coated catheters,[8] and may increase bacterial drug resistance,[9] silver ions can produce local toxic side effects[10] and the decrease in silver ions and formation of calculi on the catheter surface affect the release of the silver, and thus limit the antibacterial duration and effect.[11] A new type of silver alloy hydrogel-coated (SAH) catheter has recently entered the healthcare market, with a gold, silver, and palladium coating. This catheter has been shown to prevent bacterial adhesion and colonization by generating a microcurrent and blocking the retrograde infection pathway, without producing any significant toxic components.[12] The largest randomized controlled study of SAH catheters to date (27,878 patients) showed that it promoted a 32% reduction in the risk of urinary tract infections and a 21% reduction in the incidence of CAUTIs, while the incidence of secondary blood infections was reduced by 44% and the number of all infecting microorganisms was reduced.[13] However, these studies rarely targeted critically ill patients and the ability of this catheter to reduce the incidence of CAUTIs in critically ill patients has not been verified. Notably, patients in ICU tend to have immune system disorders, widespread use of antibiotics, and proliferation of drug-resistant bacteria, making it necessary to re-evaluate the efficacy of SAH catheters for preventing CAUTIs in these patients. We therefore conducted a prospective, randomized, controlled study to evaluate the effectiveness of this SAH catheter for preventing bacteriuria and CAUTIs in critically ill patients with indwelling catheters and to evaluate the formation of biofilms on the catheter surface using a semi-quantitative colony-counting method.

Methods

Patient population

This prospective single-center, single-blind, randomized, controlled study was conducted in the ICU of the First Affiliated Hospital of the University of Science and Technology of China (Anhui Provincial Hospital) from October 2022 to February 2023. The study included critically ill patients aged ≥18 years in the ICU who required indwelling catheterization. Patients who met any of the following criteria were excluded: (1) estimated time of indwelling catheter <14 days; (2) long-term use of glucocorticoids or immunosuppressive drugs; (3) malignancy; (4) hematological diseases; (5) autoimmune diseases or immunodeficiency; (6) history of structural urinary tract diseases (like prostatic hyperplasia, urinary calculus, urethral malformation, etc.); (7) patients with indwelling catheterization for >48 h before admission; (8) urinary tract infection or latent infection before admission to ICU; and (9) acute or chronic renal function injury. Patients who meet either of the following criteria will be withdrawn from this study: (1) the enrolled patients had an indwelling catheter for less than 14 days; (2) the patient experienced intolerable adverse events, and the researchers believe that it cannot be ruled out as a result of experimental intervention; (3) serious violation of the trial protocol by patients or researchers; and (4) subjects request to withdraw from the study. All the subjects volunteered to participate in the clinical study and signed an informed consent form.

Randomization and study protocol

The patients were divided randomly into a SAH catheter group and a conventional catheter group in a 1:1 ratio according to a computerized simple random method. Patients in the SAH catheter group received an indwelling SAH catheter (BIP Foley Catheter, Bactiguard AB, Stockholm, Sweden) and patients in the conventional catheter group received a conventional indwelling siliconized latex Foley catheter (Henan Chengan Medical Technology Co., Ltd., Xinxiang, China). Urine samples were collected on days 3, 7, 10, and 14 after catheter placement for routine urine and urine culture examination. To protect the patients' interests, if CAUTIs were diagnosed, the catheter was immediately replaced and the patient received appropriate antiinfection treatment, and the observation was terminated. All remaining catheters were removed on day 14, irrespective of the presence of CAUTIs.

Observation indicators

The main outcome measure was the incidence of CAUTIs, based on the clinical and etiological diagnostic criteria in the "Hospital Infection Diagnostic Standard (Trial)" issued by the Ministry of Health of the People's Republic of China. Considering the study was not blinded to the investigators and there was a subjective judgment in the diagnosis process of CAUTIs, the diagnosis was completed by another group of senior physicians. They independently completed the diagnosis without reference

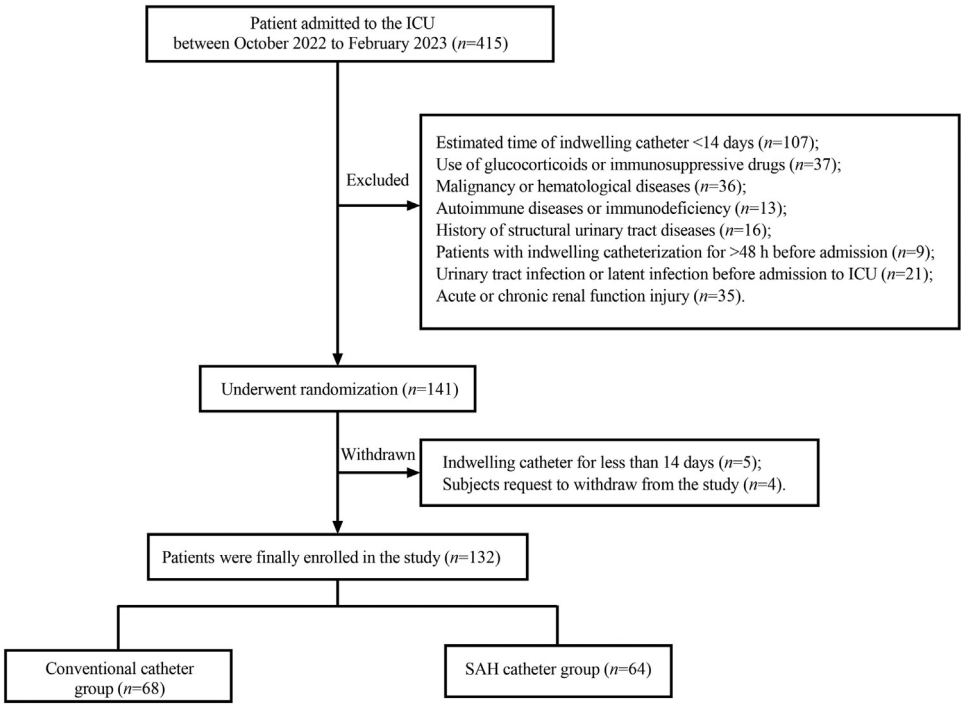

Figure 1. Flowchart of study participants. ICU: Intensive care unit; SAH: Silver alloy hydrogel-coated.

to the judgment of the patients' healthcare team. Secondary outcome indicators included the presence of white blood cells in the urine and the rate of positive urine cultures on days 3, 7, 10, and 14; the numbers of viable bacteria in the biofilm on the tip, balloon, and tail segments of the catheter; the pathogenic characteristics of positive urine cultures; length of ICU stay; overall hospital stay; ICU mortality; and the 28-day mortality rate.

Catheter biofilm viable count

The numbers of viable bacteria (cfu) in the biofilm on the surface of the catheter after removal on day 14 were determined semi-quantitatively for 10 randomly selected patients in each group, using a colony-counting method. The tip, balloon, and tail segments of the catheter were cut off in an aseptic environment, rinsed gently in 3 mL phosphate-buffered saline (five times), the surface layer of planktonic bacteria was washed off, and the catheter was placed in 2 mL Luria-Bertani (LB) broth medium (BD Difco, Franklin Lakes, NJ, USA). Adherent bacteria on the surface of the catheter were completely removed by ultrasound (250 kHz, 40% power, 15 min), mixed with 100 μL of LB broth, diluted several times in a 10-fold gradient, and 10 μL was then added into a sterile LB agar (BD Difco, Franklin Lakes, NJ, USA) plate and smeared evenly. The procedure was repeated three times in parallel and an effective concentration included 30–300 visible colonies in a single plate. The average number of visible colonies was then calculated.

Statistical analysis

All data analysis was conducted using SPSS 23.0 (IBM, Armonk, NY, USA). Measured data with a normal distribution were expressed as mean±standard deviation and compared by *t*-tests, and data not conforming to a normal distribution were expressed as median (interquartile range) and compared between groups using non-parametric tests. Numerical data were expressed as numbers (percentage) and compared between groups using χ^2 test or Fisher's exact probability methods or continuity-corrected χ^2 for classified variables. A two-tailed P <0.05 was considered a significant difference.

Results

Baseline data of subjects

A total of 415 patients were admitted to the ICU between October 2022 and February 2023. After excluding patients who did not meet the relevant criteria, a total of 141 patients were enrolled in the study. Five patients with indwelling catheterization shorter than 14 days were withdrawn from the study, and four patients requested to withdraw from the study. Finally, 132 subjects were enrolled in the study, including 68 patients in the conventional catheter group and 64 patients in the SAH catheter group (Figure 1). The baseline clinical data for the two groups are shown in Table 1. There were no significant differences between the groups in terms of baseline demographics, main diagnosis at admission to ICU, underlying disease, and laboratory examinations before randomization. In addition, 53 (78.0%) and 49 (76.6%) patients in the conventional and SAH catheter groups, respectively, had antimicrobial use <7 days before randomization, with no significant difference between the groups, and there was no significant difference between the groups in the types of antibiotics used before and after randomization, indicating that the use of antibiotics did not affect the comparability between the two groups (Table 2).

Table 1
Baseline characteristics of patients in the conventional catheter group and SAH catheter group.

Item	Conventional catheter group (*n*=68)	SAH catheter group (*n*=64)	*P*-value
Age (years)	64.6 ± 17.5	60.0 ± 18.7	0.145
Gender, female	30.0 (44.1)	28.0 (43.8)	0.966
Main diagnosis			
Pulmonary infection	18.0 (26.5)	14.0 (21.9)	0.538
Cerebral vascular accident	13.0 (19.1)	8.0 (12.5)	0.299
Trauma	2.0 (2.9)	8.0 (12.5)	0.081
Acute coronary syndrome	5.0 (7.4)	6.0 (9.4)	0.674
Acute pancreatitis	4.0 (5.9)	5.0 (7.8)	0.925
Encephalitis	4.0 (5.9)	1.0 (1.6)	0.399
Intestinal obstruction	2.0 (2.9)	3.0 (4.7)	0.945
Drug poisoning	2.0 (2.9)	3.0 (4.7)	0.945
Valve heart disease	3.0 (4.4)	1.0 (1.6)	0.655
Status epilepticus	2.0 (2.9)	1.0 (1.6)	1.000
Pulmonary embolism	2.0 (2.9)	1.0 (1.6)	1.000
Liver failure	1.0 (1.5)	2.0 (3.1)	0.958
Diabetic ketoacidosis	1.0 (1.5)	2.0 (3.1)	0.958
Others	4.0 (5.9)	4.0 (6.3)	1.000
Comorbidity disease			
Cardiovascular disease	43.0 (63.2)	37.0 (57.8)	0.524
Chronic respiratory disease	19.0 (27.9)	20.0 (31.3)	0.667
Disease of the nervous system	18.0 (26.5)	22.0 (34.4)	0.323
Diabetes	16.0 (23.5)	14.0 (21.9)	0.821
Liver disease	6.0 (8.8)	8.0 (12.5)	0.493
Others	4.0 (5.9)	5.0 (7.8)	0.925
Severity of illness at ICU admission			
APACHE II score	19.7 ± 5.7	18.1 ± 6.5	0.121
SOFA score	13.0 (11.3–15.0)	12.5 (11.0–15.0)	0.456
Laboratory examination			
White blood cell count ($\times 10^9$/L)	10.40±2.7	10.3 ± 2.7	0.787
Neutrophil percentage (%)	79.8 ± 8.6	81.2 ± 8.4	0.369
Procalcitonin (ng/mL)	2.5 (0.8–7.5)	2.5 (0.8–6.8)	0.969
C-reactive protein (mg/L)	49.9 (20.7–76.5)	48.4 (19.4–78.3)	0.845
Creatinine (μmol/L)	71.5 ± 18.4	67.5 ± 18.5	0.217

Data are expressed as *n* (%) or mean±standard deviation or median (interquartile range).
APACHE II: Acute physiology and chronic health evaluation scoring system; ICU: Intensive care unit; SAH: Silver alloy hydrogel-coated; SOFA: Sequential organ failure assessment.

Table 2
The types of antibiotics used in the two groups of patients before and after randomization.

Antibiotic	Before randomization			After randomization		
	Conventional catheter group (*n*=68)	SAH catheter group (*n*=64)	*P*-value	Conventional catheter group (*n*=68)	SAH catheter group (*n*=64)	*P*-value
Cephalosporins	25.0 (36.8)	24.0 (37.5)	0.930	19.0 (27.9)	17.0 (26.6)	0.859
β-lactamase inhibitors	15.0 (22.1)	16.0 (25.0)	0.690	22.0 (32.4)	19.0 (29.7)	0.741
Aminoglycosides	6.0 (8.8)	5.0 (7.8)	0.834	7.0 (10.3)	6.0 (9.4)	0.859
Quinolones	14.0 (20.6)	15.0 (23.4)	0.693	13.0 (19.1)	11.0 (17.2)	0.774
Carbapenems	11.0 (16.2)	9.0 (14.1)	0.735	18.0 (26.5)	17.0 (26.6)	0.990
Glycopeptides	8.0 (11.8)	7.0 (10.9)	0.881	12.0 (17.6)	13.0 (20.3)	0.696
Antifungal drugs	4.0 (5.9)	3.0 (4.7)	1.000	9.0 (13.2)	11.0 (17.2)	0.527

SAH: Silver alloy hydrogel-coated.

Positive rates of urine leukocytes, urine culture, and incidence of CAUTIs in the two groups

Figure 2 shows the rates of urine white blood cells and positive urine cultures, and the incidence of CAUTIs at 3 days, 7 days, 10 days, and 14 days after catheter placement in the conventional and SAH catheter groups. All three indicators increased with time. The positivity rates for urinary white blood cells on days 3, 7, 10, and 14 after catheter placement in the conventional catheter group were 11 (16.2%), 23 (33.8%), 29 (42.6%), and 36 (52.9%), respectively, and the rates in the SAH catheter group were 4 (6.3%), 10 (15.6%), 13 (20.3%), and 18 (28.1%), respectively. The differences between the groups were significant on the 7th day (*P*=0.016), 10th day (*P*=0.006), and 14th day (*P*=0.004). The rates of positive urine cultures on days 3, 7, 10, and 14 were 4 (5.9%), 12 (17.6%), 19 (27.9%), and 26 (38.2%), respectively, in the conventional catheter group, and 1 (1.6%), 5 (7.8%), 7 (10.9%), and 13 (20.3%) in the SAH catheter group, with significant differences between the groups on the 10th day (*P*=0.014) and 14th day (*P*=0.024). The numbers of CAUTIs on days 3, 7, 10, and 14 were 3 (4.4%), 6 (8.8%), 15 (22.1%), and 23 (33.8%), respectively, in the conventional catheter group, and 0 (0%), 1 (1.6%), 5 (7.8%), and 7 (10.9%), respectively, in the SAH catheter group, with significant differences between the groups on the 10th day (*P*=0.023) and 14th day (*P*=0.002). The incidences of CAUTIs per 1000 catheter-days in the conventional catheter group and SAH catheter group were 24.2 and 7.8, respectively.

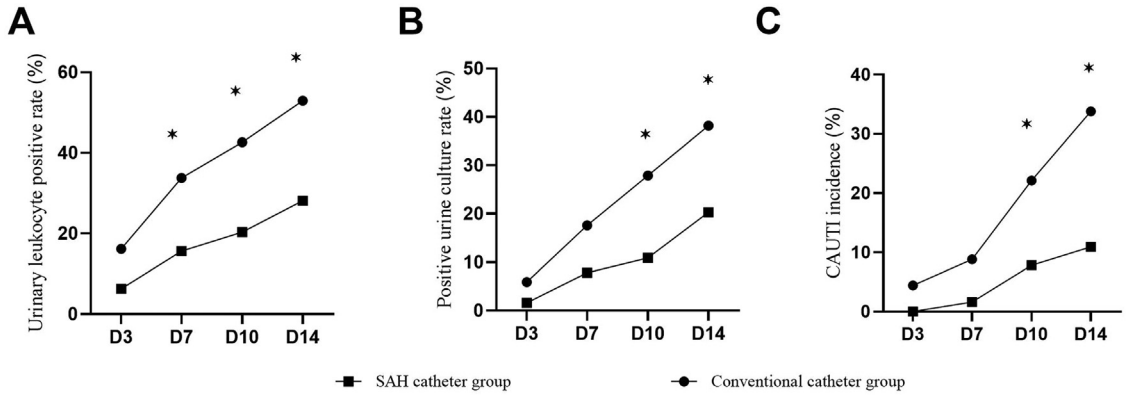

Figure 2. The rates of urine white blood cells (A), positive urine cultures (B), and the incidence of CAUTIs (C) at 3 days, 7 days, 10 days, and 14 days after catheter placement in the conventional catheter and SAH catheter groups.
*The difference between groups was statistically significant (P <0.05).
CAUTIs: Catheter-associated urinary tract infections; SAH: Silver alloy hydrogel-coated.

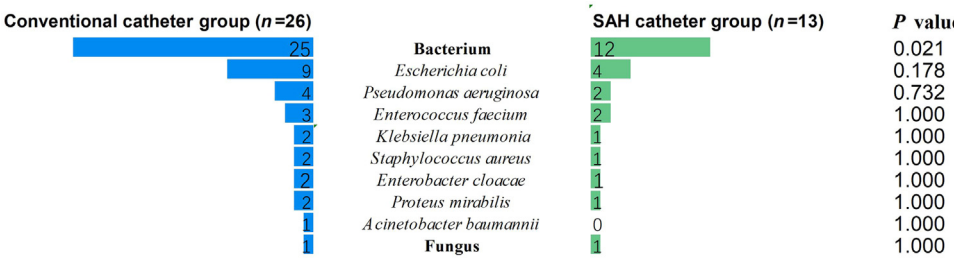

Figure 3. Distribution of pathogenic bacteria in the two groups of patients according to the urine culture. SAH: Silver alloy hydrogel-coated.

Distribution of pathogens in the two groups

Figure 3 shows the distribution of pathogenic bacteria in urine cultures in the two groups. Only one pathogenic microorganism was reported in urine cultures from each patient. Bacteria were detected in urine cultures from 25 patients in the conventional catheter group and 12 in the SAH catheter group on day 14 (P=0.021); however, there was no significant difference in specific species between the two groups (P >0.05). The most common bacteria in urine cultures in both groups were *Escherichia coli* (n=13) and *Pseudomonas aeruginosa* (n=6), with only one case of *Candida* in each group.

Bacterial colony counts in biofilms on two kinds of catheters

Viable bacteria on different parts of the catheter were counted after the removal of the urethral catheter on day 14 in 10 randomly selected patients from each group. The numbers of viable bacteria isolated from the tip, balloon, and tail segments in the conventional catheter group were $[3.21\pm1.91]\times 10^6$ cfu/mL, $[7.30\pm1.99]\times10^7$ cfu/mL, and $[6.41\pm2.07]\times10^5$ cfu/mL, respectively, and the numbers in the SAH catheter group were $[7.44\pm2.22]\times10^4$ cfu/mL, $[3.48\pm2.38]\times10^5$ cfu/mL, and $[8.50\pm1.46]\times10^3$ cfu/mL, respectively. The differences between the groups were significant for each part (P <0.001; Figure 4).

Prognosis in each group

Table 3 shows the prognosis of patients in the conventional and SAH catheter groups. There were no significant differences between the groups in terms of the length of stay (LOS) in the ICU, total LOS, ICU mortality, and 28-day mortality.

Table 3
Prognosis of patients in the conventional catheter and SAH catheter groups.

Item	Conventional catheter group (n=68)	SAH catheter group (n=64)	P-value
ICU LOS (days)	21.0 (17.0–24.8)	21.0 (17.0–24.0)	0.464
Total LOS (days)	24.5 (22.0–27.0)	24.0 (21.3–27.0)	0.601
ICU mortality (%)	7.3	5.0	1.000
28-day mortality (%)	14.5	11.7	0.881

Data are expressed as n (%) or median (interquartile range).
ICU: Intensive care unit; LOS: Length of stay; SAH: Silver alloy hydrogel-coated.

Discussion

The current study included 132 critically ill patients and compared urinary white blood cells, urinary cultures, and the incidence of CAUTIs between patients receiving conventional and SAH catheters. Although most of the patients received anti-infective therapies before catheterization, the above indexes were still increased in both groups on the third day after catheter insertion, with no significant advantages of the SAH compared with the conventional catheter at this time. On the 7th day, however, the incidence of urinary white blood cells was significantly higher in the conventional catheter group compared with the SAH catheter group, providing the earliest indication of a significant difference between the two groups. By the 10th day, the positive urine culture rate and incidence of CAUTIs were both significantly reduced in the SAH catheter group compared with the conventional catheter group. SAH catheters thus reduced the incidence of CAUTIs in critically ill patients in clinical practice

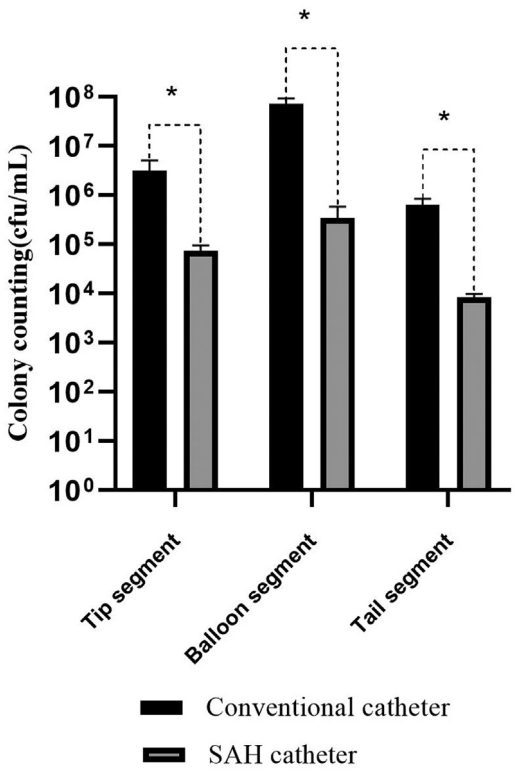

Figure 4. Bacterial colony counts in biofilms on different parts of the two kinds of catheters after removal of the urethral catheter on day 14. *The difference between groups was statistically significant (P <0.001). SAH: Silver alloy hydrogel-coated.

compared with conventional siliconized latex Foley catheters, but the effect may not become significant until around 1 week after catheterization. Although the advantages of SAH catheter must be recognized, we should also realize that it is possible to effectively prevent CAUTIs by replacing conventional urinary catheters in the short term.

Urine cultures detect free bacteria in the urine. There was no significant difference between the two groups in terms of the types of pathogenic microorganisms, suggesting that SAH catheters inhibit a wide range of microorganisms, consistent with the study by Chung et al.[12], Aljohi et al.[14], and Rupp et al.[15] However, only one patient's urine from each group cultured fungi, and we were therefore unable to judge whether or not SAH catheters can effectively inhibit the growth of fungi.

Biofilms are communities of sessile bacteria that adhere to biotic or abiotic surfaces and are protected by a polymeric matrix generated by the bacterial cells.[16] Biofilm-associated infections are difficult to treat, and microorganisms in catheters are less susceptible to antimicrobials than their planktonic counterparts.[17] Understanding the formation of biofilms on the surface of catheters is therefore important for preventing and reducing CAUTIs. Bacterial biofilms on SAH catheters have only been investigated *in vitro* to date, and SAH catheters were shown to reduce bacterial colonization *in vitro* by 60% after 30 days, compared with conventional catheters.[18] Further, *in vivo* studies and clinical trials of the inhibitory effects of SAH catheters on biofilm are required. In clinical practice, most critically ill patients will be exposed to broad-spectrum antibiotics, which can inhibit free bacteria but may also disturb the balance of the urogenital microbiome and promote the propagation of specific microorganisms to produce biofilms.[19] The pathogenic microorganisms cultivated from the middle urine in this study included *E. coli, P. aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii, Enterococcus faecium, Staphylococcus aureus*, and *Candida* (Figure 3), almost all of which have strong abilities to form biofilms.[20] We compared the formation of bacterial biofilms on the surfaces of the two kinds of catheters after 14 days, and showed that SAH catheters had significantly fewer viable biofilm bacteria on different parts of the catheter compared with conventional catheters, indicating that SAH catheters can effectively inhibit the formation of bacterial biofilms.

Although SAH catheters are widely recognized to reduce CAUTIs and inhibit the formation of bacterial biofilms, the current results showed no difference in hospital stay or mortality between the SAH catheter and conventional catheter groups, which seems to contradict the conclusion that CAUTIs contribute to increased patient mortality. This apparent discrepancy may be attributed mainly to the fact that SAH catheters only reduced the incidence of CAUTIs by 22.9% during the observation period, and this protective effect may thus not be reflected in the prognosis.

This study had some limitations. First, it was a single-center study with a limited sample size. Second, although we tried to ensure the consistency of the baseline data between the two groups of patients, the disease types were not limited, and heterogeneity between the patients may thus have led to a selection bias. Following the request of the Ethics Committee of the Research Center, the indwelling catheterization time should not exceed 14 days. However, insufficient intervention may lead to bias on some prognostic indicators, such as mortality and length of ICU stay.

Conclusions

In conclusion, this prospective, randomized controlled trial showed that the SAH catheters could effectively reduce urinary bacteria, reduce the incidence of CAUTIs, and inhibit the formation of catheter-related bacterial biofilms in critically ill patients compared with conventional catheters; however, it is still necessary to replace the catheter regularly, irrespective of the catheter material.

Author Contributions

Menglong Zhao: Methodology, Data curation, Writing – Original draft preparation. **Shike Geng:** Methodology, Data curation. **Lei Zhang:** Visualization, Investigation. **Xiaoqin Fan:** Methodology, Data curation, Formal analysis. **Fei Tong:** Methodology, Data curation. **Xianlin Meng:** Methodology, Data curation. **Tianfeng Wang:** Methodology, Data curation. **Xiaowei Fang:** Methodology, Data curation. **Qing Mei:** Supervision, Visualization, Project administration. **Aijun Pan:** Conceptualization, Supervision, Visualization, Project administration.

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Ethics Statement

This study was conducted after an agreement from the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (Ethics No: 2022-ky163) and registered in the China Clinical Trial Registration Center (registration No: ChiCTR220065484). Each patient who participated in the survey provided a signed informed consent form or had a family member sign an informed consent form. In general, all data in this study were obtained in accordance with the Helsinki Declaration.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. All the authors of the manuscript have agreed to publish.

Data Availability

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

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